ARCHIVES of OPHTHALMOLOGY

Volume 2 OCTOBER, 1929 Number 4

THE INTERNATIONAL CONGRESS OF OPHTHALMOLOGY *

GEORGE S. DERBY, M.D.

BOSTON

Twenty years ago, the twelfth International Congress of Ophthalmology was held in Lucerne. The thirteenth, originally planned for St. Petersburg in the summer of 1914, was prevented by the World War. Ten years elapsed following the armistice before it was possible to gather the ophthalmologists of the world together. The stage was set in Amsterdam, the time September 5 to 13, and except for an occasional shower the sun shone brightly each day.

A vast amount of preliminary spade work had been done by the Dutch colleagues Zeeman, Marx, van der Hoeve, Rochat, Weve, Mulock-Houwer, Roelofs and many others. There was a central registration hall at the Kolonial-Institut, in which building the exhibits were installed and many of the meetings held. Here each member had his own private box in which all notices and correspondence were placed each day, here was a banking office, the executive offices of the Congress, etc. Here at the central desks was to be found a bevy of charming and efficient young women, who spoke English, French and German and heaven knows what other languages, who answered all inquiries and smoothed out the various difficulties which always arise for the stranger in a foreign country. Indeed, the opportunity to meet and converse with these attractive young women more than compensated for the long journey.

The members registered on the morning of September 5, and in the afternoon the Congress officially opened with a general gathering in the Concert House. The organ opened with the national air, the audience rose, and the Queen Mother, who is greatly beloved, entered with her escort. Professor van der Hoeve opened the proceedings with a short speech of welcome, first in Dutch, then in English, French, German, Italian and Spanish. The Queen Mother then made a short speech of welcome, first in Dutch and then in French. Graceful replies were then made by the representatives of different nations, Parsons for Great Britain, Terrien for France, Krückmann for Germany, Dalén for the Scandinavian countries, Wilmer for America, etc. The proceedings

* Submitted for publication, Oct. 3, 1929.

were brief and dignified, and were followed by a general reception and tea in the Pavilion Vondelpark, an attractive restaurant in a park, where many greetings were exchanged and friendships renewed. In the evening, representatives of each country met to consider the reports which were presented to the Congress, on various subjects: standardization of visual acuity, education of ophthalmologists, the light sense, standards of perimetry, visual standards for aviators and others. The division that I attended was admirably presided over by Professor Nordenson, and developed a number of interesting discussions. Nordenson made all his announcements fluently in English, French and German, and all remarks were translated when the occasion required. Each speaker in this meeting, as well as in the scientific proceedings of the Congress, was required to write out an abstract of his remarks for the secretary.

On Friday morning, September 6, the real business of the Congress began with a general meeting in the large hall of the Kolonial-Institut, Treacher Collins of England, the President of the Congress, in the chair, with van der Hoeve speaking all the languages at his elbow and making all the announcements in English, French and German. The morning was taken up with demonstrations, a few of which might be mentioned: first, fundus photography, colored and otherwise, which was somewhat disappointing; excellent movies of cataract extraction, in black and white by Elschnig and in colors by Wessely; a demonstration of a Zeiss modification of the Gullstrand ophthalmoscope by which an instructor and eight students can all look simultaneously at the same fundus.

In the afternoon a discussion on glaucoma was held, the reporters being Duke-Elder of London, Hagen of Norway, Magitot of France, and Wessely of Germany. There were no loud speakers for the large hall, and few could make themselves well heard throughout. About 250 communications were presented to the Congress, and owing to the large number it was necessary to divide into three sections on each of the three succeeding days in order to give everyone a hearing. No one man, unless divided into three, could follow all, and so it became necessary to pick and choose the papers of particular interest, not forgetting that hours of profitable time could be spent in examining the various instruments and exhibits. The papers will soon be available for all to read.

On Saturday afternoon and Sunday, free excursions to many of the points of interest in this small but delightfully interesting country were provided and were enjoyed by most of the members and their families. While the sessions were being held many trips were enjoyed by the women and children, and it can be truly said that this extensive and generous entertainment was one of the most enjoyable features of the meeting and will hardly be equaled in congresses of the future. The

excursions along the canals were especially delightful and, of course, to most of the members quite unusual.

A meeting of this sort provided a wonderful opportunity to see the great men with whose names we have long been familiar in the literature. The Grand Old Man of the occasion was Fuchs, beloved of all, looking a little older, perhaps, than when he was in the United States, but still alert and brimming over with good fellowship and keen humor. A luncheon, organized by Dr. Suker, was tendered him on September 10, and was attended by about 100 men, many of them his old American students, also a number of distinguished men of other nations. Felicitous speeches were made by representatives of the various nations, and a fine note of friendship and good fellowship was struck. The Hofrat's reply was worthy of the man and was greeted with great applause.*

Among the well known men present at the Congress a few may be mentioned: from Germany and Austria, Axenfeld, Wessely, Krückmann, Wagenmann, Hertel, Elschnig, Meller and Lindner; the French had Morax, Terrien, Rochon-Duvigneaud, Dupuy Dutemps and Magitot; the English, Treacher Collins, Parsons, Lister and Duke-Elder. Col. R. E. Wright came all the way from Madras; the United States must have had a representation of from seventy to eighty men, from Massachusetts to California and from Texas to Minnesota. There were many Scandinavians, Italians, Spanish and South Americans, with a plentiful sprinkling from the small countries. It was reported that although efforts had been made to obtain a representative group of Russians, only one man was deemed sufficiently sound in his views to be trusted to resist the contamination of the outside world. It is said that all others were refused permission to attend by the Soviet government.

After the Sunday rest, the Congress in its three sections industriously waded through its formidable program. On Monday evening, a brilliant reception was held in the Amsterdam palace, at which the Prince Consort was present, and on Tuesday evening a small group was received by the Queen Mother in her residence at Soestdyk. On Wednesday we packed our bags and the Congress adjourned by land and water to Scheveningen, a beach resort with large hotels, a theater and a Kurhaus, which is really a suburb of the Hague. On Wednesday night, a reception in the famous Ridderzaal at the Hague took place. Thursday and Friday were the last two days, and again the Congress met as a whole, the bulk of communications having been disposed of. Two discussions were of especial interest, one on angiomatosis of the retina, at which Arvid Lindau, a modest young Swede, appeared. It will be remem-

* The Leslie Dana Medal was presented to Professor Fuchs at this luncheon.

bered that his brilliant paper in 1926 added much to the knowledge of this interesting condition. The second feature of interest was the discussion of Gonin's technic in the cauterization of retinal separation. Each speaker added his testimony as to the value of this procedure in an appreciable percentage of cases. Gonin showed many convincing pictures of the fundus in his cases before and after operation. Gonin himself, now acclaimed as the discoverer of a useful addition to operative technic, spent most of his time in taking cracks at his previous critics. In the afternoon came the eagerly awaited symposium on suprasellar tumors, the chief event of which was Cushing's admirable paper, which unfortunately had to be considerably abbreviated. As the Congress neared its end the attendance tended to diminish as the other attractions of the Hague and its surroundings exacted their toll. In the evening came the great banquet in the Kursaal, attended by hundreds and much enjoyed by all. On Friday came further papers and the finale, but of this I cannot report as, in company with a number of others, I had to leave in order to catch the boat sailing Saturday for this country.

Altogether the thirteenth International Congress was a notable occasion, and the kindness, courtesy and hospitality of the Dutch hosts will not soon be forgotten.

INTRACRANIAL ANEURYSMS

THEIR RÔLE IN THE PRODUCTION OF OCULAR PALSIES *

ADOLPH O. PFINGST, M.D.
AND
R. GLEN SPURLING, M.D.
LOUISVILLE, KY.

Our purpose in this report is to call attention to the frequent occurrence of ocular palsies in cases of aneurysm of the basal cerebral arteries. Our information was derived from a detailed review of the literature and the study of two cases so diagnosed during the life of the patients. In an analysis of 5,432 autopsies in 1916, Fearnsides [1] made the interesting and surprising observation that saccular or fusiform aneurysms of the basal vessels of the brain were present 44 times. He pointed out that the clinical history in these cases indicated frequent involvement of the motor nerves of the eyes. He also quoted Osler's [2] statistics of 12 instances of basal cerebral aneurysm occurring in 800 autopsies and Pitt's,[3] of 23 instances in 900 autopsies. These figures would indicate that basal aneurysms are more frequent than is generally supposed.

The relative frequency with which the arteries at the base of the brain are involved can be gleaned from Gowers' [4] summary of 154 reports of cases of basal aneurysm taken from the literature prior to 1893, shown in the accompanying table:

Gowers' Summary of One Hundred and Fifty-Four Cases of Basal Aneurysm

Middle cerebral	44
Basilar	41
Internal carotid	23
Anterior cerebral	14
Anterior communicating	8
Posterior communicating	8
Vertebral	7
Posterior cerebral	6
Inferior cerebral	3
Total	154

These figures seem to agree in a general way with subsequent statistics.

* Submitted for publication, June 20, 1929.

1. Fearnsides, E. G.: Brain **39**:224 (Oct.) 1916.
2. Osler: Principles and Practice of Medicine, New York, D. Appleton & Company, 1912, p. 982.
3. Pitt, Newton: Brit. M. J., 1890, p. 827.
4. Gowers: Diseases of the Nervous System, Philadelphia, P. Blakiston's Son & Company, 1893, p. 529.

The diagnosis of intracranial aneurysm during life has always been considered difficult, in fact, almost impossible except in a conjectural way. Fearnsides, like all of the earlier observers, concluded that a positive diagnosis of cerebral aneurysm during life is impossible. His studies were all made post portem, the clinical symptoms being considered altogether in retrospect. The interesting observation was made by Fearnsides that all of the cases which have evidenced pressure symptoms revealed a leak in the wall of the aneurysm and a coincident clot ("false aneurysm"), and that there had been an absence of symptoms in the cases in which rupture had not occurred.

Although numerous cases of aneurysm of the basal vessels have been reported by pathologists since Fearnsides' publication, little progress has been made in their clinical study until recent years. The advent of the neurosurgeon and the consequent frequent exploration of the cranial cavity, with a coincident growing interest in intracranial pathologic conditions not only has been the impetus to the clinical study of intracranial conditions as a whole, but has led to a more definite means of diagnosis of basal cerebral aneurysm; thus, the assumption that aneurysms of the basal arteries are not infrequently associated with ocular palsies has been verified. The study of cerebral aneurysms has been encouraged, especially by Cushing, who looks on this lesion as one of the most frequent causes of sudden paralysis of the oculomotor nerves. In recent years, he and his co-workers have made valuable contributions to the literature on this subject. In a contribution from the Cushing clinic, Albright [5] reported two cases in which a diagnosis of intracranial aneurysm was made during life, in one of which the condition was confirmed at necropsy. He abstracted from the literature reports of twenty-nine other cases in which the clinical diagnosis was made possible in every instance and in all of which the condition was confirmed by operation or autopsy. Symonds [6] reported five cases from Guy's Hospital in 1923, in which the diagnosis of basal aneurysm was made during life and in two of which the condition was confirmed at necropsy.

In an endeavor to impress the importance of the rôle which intracranial aneurysms play in the production of the ocular palsies, letters of inquiry were addressed to a number of prominent neurologic surgeons in this country regarding their view as to the frequency of lesions of this kind. With only one or two exceptions, the replies stated that cases of aneurysm associated with oculomotor paralysis had been diagnosed, in some of which the diagnosis had been verified by surgical

5. Albright, Fuller: Bull. Johns Hopkins Hosp., April, 1929.

6. Symonds, C. P.: Guy's Hosp. Rep., 1923.

exploration or at necropsy. Most of the replies indicate an increasing tendency to consider basal cerebral aneurysms in the etiology of ocular palsies and a growing conviction that though they perhaps represent one of the less frequent causes of acquired ocular paralyses, their rôle as an etiologic factor is an important one.

Fuchs classified ocular palsies according to the anatomic position of the lesion into extracranial or orbital and intracranial. He divided the intracranial lesions into those affecting the higher levels, i.e., the nuclei or the nerves between the nuclei and their exit from the brain surface (fascicular) and those affecting the lower level or the nerve trunks at the base, i.e., between their exit from the surface of the brain and their entrance into the orbit. In the latter category must be placed the lesions resulting from cerebral aneurysms. Symonds classified the symptoms of basal aneurysms into those due to mechanical pressure on surrounding structures (neighborhood symptoms) and those peculiar to the presence of the aneurysm itself. The close proximity of the cranial nerves to the cerebral arteries at the base would lead one to expect pressure effects on one or several of the cranial nerves when an aneurysm develops at any part of the circle of Willis.

Aneurysms of the internal carotid often reach considerable size before rupture takes place and may cause symptoms by pressure on contiguous parts. However, until an aneurysmal sac has reached considerable proportions, signs in the contiguous areas are not apt to prevail unless a break or leak has occurred in the sac. Mortuary records show that in more than half the cases of cerebral aneurysm showing ocular manifestations rupture of the sac had occurred. Such cases have a sudden onset and are usually associated with giddiness, stertorous breathing, severe headache, pain in the back of the neck radiating into the back and paralysis of one or more of the cranial nerves at the base (from the first to the eighth), varying with the site of the lesion.

A review of the topographic relations of the motor nerves of the eye at the base would perhaps lead to a better understanding of the symptomatology. Their relations are such that in the passage of the nerves from their superficial origin at the brain surface, through the dura and to their entrance into the orbit, lesions at the base or in the middle cerebral fossa may at the same time involve the third, fourth and sixth nerves and at times the trigeminus. After the exit of the motor oculi in front of the pons inside the crura, the two nerves diverge and pass between the posterior cerebral and the superior cerebellar arteries and then for about 1 cm. along the internal carotids in their course to the sphenoidal fissure. Although well separated from the third nerve at their exit from the brain, the trochlearis, abducens and trigeminus run forward and come close to the third nerve. In its

course along the carotid the third nerve lies next to the artery, the trochlearis somewhat more downward, and still further downward and outward lie the branches of the trigeminus. In part of its course, the abducens lies between the carotid and the cavernous sinus. The more exposed position of the oculomotor and its proximity to the middle cerebral, communicating and carotid vessels account for the more frequent involvement of this nerve than of the other motor nerves in lesions of the anterior group of basal arteries. It is not always affected in its entirety. Only one or more branches of the nerve may be involved, the condition thus simulating paralyses of nuclear origin. Barthalow [7] described a rather definite syndrome of symptoms in aneurysms occurring at the junction of the internal carotid and middle cerebral arteries. This syndrome, due to pressure on contiguous structures, consists of ptosis, mydriasis, squint downward and outward with retarded motility upward and inward, or, when the fourth and sixth nerves are also compressed, of a complete ophthalmoplegia. As a rule there is severe pain in the face due to involvement of the ophthalmic division of the fifth. Amblyopia or amaurosis prevails; defects in the visual field are found when the optic nerve is compressed and congestion of the eyes, slight exopthalmos and swelling of the veins of the face, when the cavernous sinus is compressed by the aneurysmal sac. Disturbance of the sense of smell occurs when the aneurysmal sac extends far enough forward to compress the olfactory nerve. Signs similar to those associated with lesions at the carotid-middle cerebral junction have also been noted when the aneurysm involves the anterior communicating or the anterior cerebral vessels.

Aneurysms of the posterior part of the circle of Willis seldom reach a large size before they rupture; hence, signs of pressure on contiguous parts are as a rule not noted before the advent of apoplectiform seizures. The basilar and vertebral arteries are the most frequent of the posterior vessels to be involved. Aneurysmal lesions of these vessels infrequently affect the third or fourth nerves but involve the nerves farther back, more especially the fifth and sixth. The seventh and eighth cranial nerves may also be affected.

A large proportion of the cases of aneurysm in which rupture had occurred were characterized by a gradual extenuation of symptoms followed by relapses, the result of an intermittent leakage from the sac. Among Fearnsides' cases were several in which apoplectiform seizures had occurred at irregular intervals, in which the autopsy revealed the clotted blood in strata, indicating periodic hemorrhage of the aneurysmal sac. It seems that the interval between the seizures varies from several months to a number of years; in some cases the condition clears up entirely between attacks, while in others the symptoms merely relapse.

7. Barthalow: Am. J. M. Sc. **64**:373, 1872.

Commenting on these symptoms, Harry Lee Parker [8] expressed the view that the general behavior in cases with intermittent leakage of blood is characteristic and diagnostic of a large percentage of cases of intracranial aneurysm and hence makes it possible to recognize the disease during life. These cases clinically resemble recurrent palsies of the third nerve, the so-called migraine palsies, which were first described by Gubler in 1860. In this condition, the third nerve becomes paralyzed, usually in all of its branches. The paralysis that is ushered in with severe migraine or hemicrania also infrequently includes the fourth and sixth nerves. Entire or partial recovery takes place in from a few days to several months, to be followed by recurrence of symptoms at intervals varying from several weeks to a number of years. This condition has always been of obscure genealogy and has been attributed to syphilis, rheumatism, disease of the accessory sinuses, etc. The symptoms usually increase in severity with succeeding attacks and may finally terminate in permanent palsy. It would be reasonable to assume that many of the cases described as migraine palsies could be accounted for by a ruptured cranial aneurysm with recurrent leakage.

The radiating pain in the back of the neck which usually ushers in attacks of aneurysmal leakage and which was formerly not understood is now generally believed to be caused by an irritative meningitis due to the presence of blood in the subarachnoid space and may be classed with the symptoms peculiar to the presence of the aneurysm itself.

The presence of blood in the spinal fluid can be demonstrated in practically every case of ruptured aneurysmal sac when the fluid is examined from twenty-four to forty-eight hours after the initial symptoms. Its demonstration furnishes a most important diagnostic sign of cranial aneurysm. Later, the spinal fluid becomes xanthochromic. The positive Kernig sign so frequently noted in leaking cerebral aneurysm furnishes a valuable aid to diagnosis.

In differentiating between ocular palsies due to basal aneurysms and those due to other lesions, the paralyses due to syphilis should, perhaps, on account of their great frequency, receive first consideration. In young patients, syphilis probably accounts for more than half of the ocular palsies. It affects mostly the optic and the oculomotor nerves, seldom the fourth and sixth nerves. Autopsies have shown that syphilitic deposits between the crura and the pons are frequent, hence the frequency of palsies of the third nerve. Bilateral involvement of the oculomotor nerves is especially significant of its syphilitic origin. The symptoms in these cases usually appear more insidiously than do those due to aneurysm, and as a rule they are not associated with severe

8. Parker, Harry Lee: Aneurysms of Cerebral Vessels, Arch. Neurol. & Psychiat. **16**:728 (Dec.) 1926.

headache, pain and stiffness in the neck and back. They usually do not show a positive Kernig sign, and the spinal fluid does not contain blood.

Meningitis associated with exudation of the suppurative, tuberculous or cerebrospinal type frequently involves the nerves to the ocular muscles. The exudate usually accumulates near the chiasm and thus chiefly involves the third and sixth nerves. These cases are differentiated by the pyrexia and other constitutional symptoms and by studies of the spinal fluid.

Tumors at the base, springing from the bone or periosteum or more especially from the hypophyses, may involve the motor nerves of the eye in their lower level, and thus resemble aneurysm before rupture. The third nerve, owing to its proximity to the pituitary body and its exposed position at the level of the posterior clinoid process, is especially vulnerable in these cases.

Abscess or tumor within the brain substance of the temporal lobe may by virtue of the increase in size of the convolution and its consequent pressure on the nerves bring about ocular nerve palsies. Those due to neoplasms are usually slower in their onset than aneurysmal palsies; they are not ushered in with sudden severe headache and backache, and the spinal fluid does not show the presence of blood.

Fractures at the base, gunshot wounds and acute and chronic infectious diseases should not be lost sight of in a consideration of the etiology of ocular palsies.

REPORT OF CASES

We have recently observed two cases of ocular nerve palsy in which the clinical and laboratory evidence would justify the diagnosis of cerebral aneurysm.

CASE 1.—*History.*—A merchant, aged 40, was brought to the Louisville City Hospital in an unconscious state on July 27, 1926. The following family history was obtained: Two years prior to admission, he suffered with severe headache and "drooping" of the left eyelid. The eyes were "out of focus" during this attack. These symptoms subsided after a period of ten days. He has continued to have rather severe headaches at intervals of from five to seven days ever since this time. Three weeks before admission, the patient was seized with a sudden sharp severe pain in the head. Within a few hours, he complained of double vision. Ptosis of the left eyelid was noted. After about a week the headache became less severe, and the eyelid could be partially raised. Double vision persisted. He was able to attend to his usual duties. On the day of admission, he was found unconscious on the street beside his automobile. He had no recollection of the events just prior to this attack. The family and past history were irrelevant. He had had repeated gonorrheal infections but said that he had not had even the symptoms of syphilis.

Physical examination showed: Mild mental confusion, especially as to time and place; complete ptosis of the left eyelid; rotation of the left eye outward and slightly downward and loss of motion in every direction except outward; slight exophthalmos of the left eye; widely dilated and fixed left pupil. Ophthalmoscopic examination showed an obliteration of the outlines of the optic disk. Vision in the left eye was 20/100. Perimetric study was not possible. There seemed to be entire loss of accommodation. Lumbar puncture gave a uniformly bloody fluid

under 130 mm. pressure. The Queckenstedt test was negative. Repeated Wassermann reactions of the blood and spinal fluid were negative. The colloidal gold curve was negative. A cell count of the spinal fluid showed: red blood cells, 214,000 per cubic millimeter; white blood cells, 800 per cubic millimeter.

The neurologic examination gave negative results, except for the ocular signs, moderate involuntary rigidity of the muscles of the neck and a positive Kernig sign. Roentgen examination of the skull was reported negative.

Following the first lumbar puncture, the patient's condition improved. This procedure was repeated daily. The character of the fluid changed from blood tinged to xanthochromic. The spinal fluid pressure gradually increased, however, and after ten days it registered 250 mm. At this time the patients mental confusion became more pronounced and the headaches more severe. Ophthalmoscopic examination showed a moderate papilledema (2 diopters). He had several light, generalized convulsions in rapid succession and sank into a semicomatose state. A right subtemporal decompression was performed (Spurling). Treatment with repeated lumbar punctures and hypertonic solutions was continued. A stormy convalescence ensued.

Follow-Up Notes.—Five months later a report stated that the patient was in splendid health and was working every day at his usual occupation. Paralysis of the third nerve still persisted, though it was now incomplete; the pupil was approximately of normal size; slight ptosis persisted. The eyeball could now be rotated toward the midline and upward. There was slight pallor of the optic disk. Vision in each eye was 20/50. The visual fields showed some concentric constriction.

A recent communication from the patient, two and one-half years after the operation, stated that his general health was excellent. The ptosis had completely disappeared. Double vision persisted when he looked to the right. The eyeball could not be moved completely toward the midline. The pupil was said to be of normal size.

This case is considered one of aneurysm of the basal arteries, presumably of the posterior communicating artery. The sudden attacks of headache followed by loss of consciousness were probably due to a small perforation of the aneurysmal sac. That there was actual intracranial bleeding was attested by the fact that the spinal fluid was grossly bloody on repeated examinations. The signs of increased intracranial pressure were interpreted as being due to irritative meningitis caused by the extravasation of blood into the cerebrospinal fluid.

Case 2.—*History.*—W. L., a housewife, aged 54, presented irrelevant family and past histories. Two years before, when apparently in perfect health, she was seized with a sudden severe right-sided headache. Within a few hours of the onset of the headache, she noticed double vision. Twelve hours later, she found it impossible to open the right eyelid. The headache, double vision and ptosis persisted for five days and slowly cleared up. There were no other symptoms referable to the nervous system during this attack. Since that time she has suffered from repeated attacks of right-sided headache, never comparable to the first seizure in severity. She considered herself in good health until three weeks before admission, when she was again seized with severe headache, which was sudden in onset and was soon followed by double vision and ptosis of the right eyelid. During this attack, the neck became sore and stiff. She was confined to bed because of the headache and stiffness of the neck. She was irrational

part of this time. After ten days the headache subsided, but the ptosis of the eyelid remained complete. Twelve days after the onset of these symptoms, examination elicited the following: complete ptosis of the right eyelid and crossed diplopia. The right eyeball was turned outward and slightly upward. It could not be rotated inward beyond the median line. Rotation downward was also limited. The pupil was moderately dilated and did not respond to light. Vision in each eye was 20/100, with correcting lenses. (A high degree of corneal astigmatism accounted for the functional defect). Examination of the visual field with a 1 mm. objective 1,000 mm. from the perimetric screen showed a superior temporal quadrant defect in the left field and an almost total loss of vision in the temporal field of the other side.

There was some involuntary rigidity of the muscles of the neck. Spinal puncture performed on the fourteenth day of the illness showed the fluid to be clear and under 150 mm. of pressure. Chemical and serologic examinations of the fluid gave negative results. The Wassermann reaction of the blood was negative.

Roentgen examination of the skull revealed a calcified area lying just to the right of the posterior edge of the pituitary fossa. This calcified shadow was interpreted by Dr. M. C. Sosman from the Peter Bent Brigham Hospital of Boston and Dr. Joseph C. Bell of Louisville as being probably due either to a deposit of lime salts in the wall of an aneurysm or to a natural calcification of a small hemorrhagic area. The pituitary fossa was normal in size and contour. The remainder of the neurologic examination gave negative results. The patient's general condition improved rapidly, and she left the hospital after a few days. The ptosis of the eyelid and the extra-ocular palsies persisted for a period of two months and then slowly subsided. At the time this paper was written, there was no diplopia and no demonstrable weakness of the third or fourth cranial nerves.

The only evidence lacking in this case to make a diagnosis of aneurysm of the basilar artery complete is the fact that the spinal fluid showed no evidence of recent blood. As the first spinal puncture was performed two weeks following the onset of the trouble, it is conceivable that a small amount of blood may have been absorbed. The calcified areas shown in the roentgenograms corresponded perfectly to the anatomic position of the third nerve.

SUMMARY

In this brief report, we have offered nothing new; in fact, our cases, even though they gave every clinical evidence of cerebral aneurysm, lack the corroborative observations obtained at operation or at necropsy to make them a valuable contribution to the literature. However, with the conviction that the diagnosis of basal aneurysm is rarely considered in ocular paralyses, we hope in the report to impress more especially the oculist with the fact that a certain percentage of ocular palsies are caused by basal cerebral aneurysms and that their presence may often be determined with a reasonable degree of certainty. We hope that the report will, in the obscure cases of ocular palsies, especially those showing apoplectiform symptoms, stimulate postmortem study of the base of the brain, particularly of the region of the circle of Willis.

DOES KERATOMALACIA EXIST IN ADULTS*

ARNOLD PILLAT, M.D.
PEIPING, CHINA

Concluded from page 287

COMMENT

These six cases represent an uninterrupted line from simple xerosis epithelialis conjunctivae to those forms of xerosis epithelialis corneae, rare in western countries, which may at any time develop into keratomalacia of adults if improper nourishment continues. It is interesting to note how the xerosis of the conjunctiva may completely leap over the limbus corneae and settle somewhere in the center of the cornea, generally in more or less sphere-shaped plaques (case 1). More frequently it happens that the xerosis of the conjunctiva pursues its course "per continuitatem" on the cornea, covering it completely or in part. My conception of Bitot's spots, which in Western countries are rarely found anywhere but in the region of the palpebral fissure, make comprehensible a disease of the cornea in that region or at least in the lower half of the cornea. Cases 1 and 3 of this series, however, show that xerosis of the conjunctiva and also of the cornea may develop under the protecting upper lid and confine itself to this area. It is also interesting to note that in two cases (cases 2 and 3) the xerosis at first adhered to those areas which had suffered changes caused by old inflammatory corneal processes and which could not be considered quite normal histologically. It can well be understood how easily, on the site of scars to which the epithelium has not adhered as firmly as it does to the normal Bowman's membrane, exfoliation of the xerotic epithelium may happen and a secondary infection may result in keratomalacia (case 2). The question of the existence of keratomalacia in adults is best answered by those cases which show a typical epithelial xerosis conjunctivae in one eye and keratomalacia proper in the other (case 4). Cases 5 and 6 prove that this dangerous disease can easily attack both eyes of adults and cause their destruction as well as it does in infants.

In view of the foregoing observations and the references in the literature, there is no doubt that keratomalacia in adults exists and that the symptoms in the eyes are analogous to those in children. Keratomalacia of adults is also closely allied to "xerosis with or without hemeralopia," found also in Europe and America, and represents in fact the last stage of its development in adults.

* Submitted for publication, May 15, 1929.

* From the Department of Ophthalmology, the Peiping Union Medical College.

As the symptoms of the disease in adults are far more easily studied and do not succeed each other so swiftly as in children, in whom perforation of the cornea may take place sometimes in a few hours, and as the interval between the first appearance of the xerotic conjunctiva and corneal complications is much shorter, I shall discuss some clinical symptoms of keratomalacia in adults not mentioned in the textbooks.

The entire disease is a noninflammatory malady of the visual organ, and therefore inflammatory redness and swelling of the lids is at first as completely absent in the new-born child, as in the adult. If these are present they are due to secondary infections of the skin of the lids, such as hordeola or furuncles. The development of these infections is promoted by the changed condition of the epithelial cells of the skin and by the relaxation of the activities of the cutaneous glands. From epithelial preparations procured by scraping the skin with a platinum spatula I have found that the skin of these patients is much richer in bacteria—in most cases staphylococci—than that of the normal person. So far, there has been no systematic examination of the bacteria of the skin in cases of keratomalacia in adults. The margin of the lid is generally pale and somewhat dry, with scaly formation around the cilia. The secretion of the conjunctival sac, practically always present in a mild degree, is not an essential symptom of the disease; it is due to a reaction of the conjunctiva to the germs, staphylococci, xerosis bacilli, diplobacilli-Morax-Axenfeld, pneumococci and streptococci flourishing thereon extensively as a result of the lowered vitality of the epithelial cells.

The conjunctiva of the lid either takes no part in the process, thus contrasting strikingly with the diseased part of the eye, or, if the disease continues for any length of time, the conjunctiva of the lids is yellowish red with an uneven surface and occasional follicles. In severe cases of keratomalacia of adults, the structure of the blood vessels disappears by thickening of the conjunctiva, and one is often embarrassed by the doubt as to whether or not one is dealing with trachoma. The curious coloring and, exceptionally, the dry state of the conjunctiva, which is, however, generally scanty and easily overlooked, ensure the making of a correct diagnosis.

The conjunctiva of the fornices, especially of the lower fornix, passes through some characteristic changes, while the upper often appears almost normal, even in advanced stages. There are humps and folds like cloudy fused follicles, which later form stiff, grayish-red, short folds in the fornix resisting any attempt at stroking away by mechanical means. This state of the conjunctiva may lead to an incorrect diagnosis of trachoma or of hyaline degeneration. In all advanced cases, but also after prolonged cases of xerosis of the conjunctiva and cornea, the

lower fornix first becomes yellow, then changes from light gray to deep brownish gray, giving the picture of a perfect argyrosis conjunctivae. I think this discoloration, hitherto noticed in keratomalacia only by Wright [38] and Mori,[41] can probably be considered parallel to the pigmentation of the skin and mucous membrane in scurvy and morbus Addisonii. Mori [41] secured it experimentally in ophthalmia of rabbits, produced by improper nourishment, which, though it contained vitamin A, included an unfavorable mixture of inorganic salts. It is caused by the presence of chromatophores in the basal cell layer of the epithelium and is strengthened by a caplike pigment at the side of the cell nucleus facing the surface of the other cell layers. Further investigation in this matter is necessary. The discoloration is capable of readjustment and disappears with the general symptoms, though often for a long time not entirely. All hues from a barely visible yellow to the darkest brownish gray are possible.

The conjunctiva of the eyeball shows either typical Bitot's spots situated in the palpebral fissure or extensive xerosis of the remaining parts in the form of islands or one continuous layer (cases 1, 2 and 3). This xerosis is preceded by the disappearance of normal luster. It is remarkable that the worst cases (nos. 4, 5 and 6) do not often show a typical xerosis but only a loss of luster together with a leathery consistency of the conjunctiva. This fact at first sight appears contradictory, but my explanation is that the conjunctiva can only show "xerosis", i.e., a dry whitish appearance, while it retains its mucous membrane-like texture, and that the "xerosis" yields to the simple dryness of the external skin as soon as the conjunctiva takes, histologically, the form of epidermis. In severe cases, however, the two conditions may exist side by side. One of the characteristic features is the wrinkling of the conjunctiva near the xerotic spots, which extends for a considerable distance into the peripheral parts of the conjunctiva of the eyeball, but is also to be found in the xerotic area. The folds run either parallel or concentrically toward the limbus, but sometimes they represent a confused jumble. In serious cases of keratomalacia coarse folds may appear; thick dark red ring folds may surround the cornea concentrically and may also partially cover the limbus (cases 4, 5 and 6, especially case 5). These folds remain for a long time and regain the luster of the normal conjunctiva only gradually. The xerosis of the conjunctiva usually recedes through a break-up of the larger plaques into small islands, during which the affected parts may change from day to day. It is probable that the xerosis begins in a similar way, but this has not yet been established as a certainty. The

41. Mori, S.: The Pathology of the Pigmentation of Bulbar Conjunctiva in Xerosis Epithelialis Conjunctivae, J. Orient. Med., 1924, vol. 2.

yellow coloring of the bulbar conjunctiva does not reach the degree of color of the lower fornix. This pigmentation is always more marked near the fornices and gradually decreases toward the limbus. It cannot be seen clearly except in mild cases, in which the eyeball is still pale or only slightly injected. In advanced cases with a leathery bluish-mauve bulbar conjunctiva it is hidden on account of the blood color tone. It is probably still present, however, and may be the cause of the curious dark coloring of the bulbar conjunctiva (fig. 15).

The disease of the cornea either takes the form of xerotic plaques (cases 1, 2 and 3) as in the conjunctiva or turns into ulcers. There is no doubt that xerosis of the cornea and keratomalacia are only a different stage of the same disease in adults, as is the case of Bitot's spots and keratomalacia in children described by Blegvad,[24] Birnbacher [27] and others. Isolated xerosis of the cornea without ulceration in adults, as described in cases 1, 2 and 3, is relatively rare even in China and is only mentioned in the early literature. I have not often had the opportunity of observing it with the material at my disposal. Corneal xerosis, appearing either as an isolated xerosis of the corneal center or as a continuation of the xerotic conjunctival plaques growing over the cornea, also occasionally turns yellow like the conjunctiva of the eyeball. It should be noted that in keratomalacia, as in pure xerosis of the conjunctiva, the xerotic spots are occasionally distributed in an almost circular formation around the limbus, forming a more or less complete white ring round the corneal margin (cases 1 and 3). This condition may give rise to an incorrect diagnosis of pannus on account of the hyperemic vessels of the limbus, which sometimes shine through from the depth. The preference for this vascularized region of the cornea seems to show that the substances producing xerosis are conducted to the eye through the circulation of the blood, and through concentration they begin to exert a destructive influence as soon as they have penetrated through the wall of the vessels. It is therefore easy to understand that the palpebral fissure, in which air, sunlight and dust continue the irritation in the diseased conjunctiva, is the favorite site of the xerosis. In severe cases, however, I have found extensive xerosis not only of the bulbar conjunctiva but even of the limbus under the covering upper lid.

There are three main possibilities regarding the origin of corneal ulcers in this disease: 1. The ulcers develop because in parts where the epithelium is exfoliated to an abnormal extent it becomes possible for pathogenic germs, especially pneumococci and streptococci, to penetrate into normal corneal tissue, cause an inflammatory process of the cornea, and so rapidly destroy the tissue, the resistance of which has greatly diminished with the general loss of resistance. 2. The trigeminus nerve is altered primarily and independently from the epithelial process and produces the corneal ulcers and the often primarily subepithelial

infiltrates by the absence of the nutritive stimulus of the nerve. 3. The parenchyma of the cornea, i.e., its mesodermal part, becomes diseased simultaneously with the epithelium but independently of it, in a way that is still not clear.

These items will be commented on separately later.

There is no need to discuss the various conditions following the perforation of the corneal ulcers, from leukoma adhaerens to panophthalmitis and to phthisis bulbi, as they are identical with those of infantile keratomalacia or of other perforated ulcers. But there is one other part of the eye which can become diseased independently and at a comparatively early stage, i.e., the lens. During daily examination with the slit-lamp, I was able to observe an increase in dulness of the lens, not only in cases 1, 2 and 3, but also in several other severe and prolonged cases of conjunctival xerosis in adult ambulatory patients in whom the cornea was not affected. This dulness is undoubtedly caused by a decrease in luster of the anterior and probably also the posterior surface of the lens. In the corneal microscope the shagreen of the lens oscillates in a variety of browns and grays, as is occasionally seen in the lenses of persons of advanced years. I do not venture to make any statements about the shagreen of the posterior lens, as the dulness of the cornea and of the anterior surface of the lens prevents any definite opinion. As I had never before examined the patients concerned, I cannot say whether the numerous white opacities, both dot-shaped and spheric, which are found in some cases under the anterior capsules, are symptoms of the disease or are congenital like those so often found in normal lenses. From the moment that keratomalacia develops, thereby excluding any intravitam examination with the slit-lamp, it is unfortunately impossible to determine how far the degeneration of the epithelium of the lens extends, and whether a further degeneration of the parenchyma of the lens is connected with it. This should, however, receive a certain amount of attention in the future, especially in any obtainable histologic material of keratomalacia, as it coincides with the opacities of the lens described by von Szily and Eckstein [42] during experimental avitaminosis in rats, although questioned by Jess.[43]

---

42. Von Szily and Eckstein: Vitamin Mangel und Schichtstargense: Katarakte als eine Erscheinungsform der Avitaminose mit Störung des Kalkotoffwechsels bei säugenden Ratten, hervorgerufen durch qualitative Unterernährung der Muttertiere, Klin. Monatsbl. f. Augenh. **71**:545, 1923; Neuer Beitrag zur Frage der experimentellen Starerzeugung bei jungen Ratten durch Vitamin-mangel der Nahrung, Klin. Wchnschr. **4**:919, 1925.

43. Jess: Ueber kongenitale und vererbbre Staarformen der weissen Ratte, nebst Bermerkungen über die Frage des Verhaltens der Linsen bei vitaminfreier Ernährung, Klin. Monatsbl. f. Augenh. **74**:49, 1925.

A frequent characteristic of the corneal xerosis and of keratomalacia in adults is the decided numbness of the cornea, which may reach complete anesthesia. In two of the foregoing cases it was possible to touch the cornea with the finger without any reaction. Future investigations will show whether the lack of sensibility also exists in cases of severe conjunctival xerosis. In the aforementioned cases this hypoesthesia not only proves the far advanced degeneration of the epithelium and of the fibers of the trigeminus nerve terminating in the basal cells, but also suggests, because of the definite nature of the symptom, that the trigeminus probably becomes diseased independently at an early stage, and that the corneal disease commences after the degeneration of the corneal nerves and after the malnutrition of the corneal nerves has reached a certain point. The fact that the corneal nerves are of surprising thickness, as shown in systematic examinations with the slit-lamp, seems to argue that the disease of the corneal nerves takes place at an early stage.

Referring to the question of hemeralopia which has been observed in the majority of cases of epidemic xerosis epithelialis conjunctivae by all research workers, one is almost entirely dependent on the statements of the patients themselves in the cases of corneal xerosis and keratomalacia. This is because the ordinary instruments do not allow an exact determination of the light sense, when opacities in the media of the eye have set in. Of the six patients mentioned I obtained reliable information about nightblindness in only three. Patients 5 and 6 had no recollection of it, and one other patient apparently did not understand the question, possibly because the nightblindness had been absent. I have the impression that even in the cases of xerosis conjunctivae, night blindness is not found so frequently in China as, for instance, in Europe. Other authors, particularly those who have had opportunities of observing large epidemics (Wright,[38] Kirkpatrick,[39] Blegvad,[26] Birnbacher [27] and others) pointed out before this that it was not possible to assert a definite connection between xerosis and hemeralopia. Although only three of my patients were mentioned as suffering from nightblindness, this does not mean that the symptom does not exist generally in keratomalacia of adults, or that it is of minor importance. On the contrary, it should be studied in the future with more material and more suitable methods of investigation.

I prefer to leave open the question of the extent to which changes in the fundus, such as anemia of the retina, whitish-gray fundus and changes of the pigment epithelium, as mentioned by several authors, occur in corneal xerosis and keratomalacia in adults. I take this position partly because of the difficulties of the ophthalmoscopic examination when the media are opaque in the center, and partly because of the generally extremely dark fundi of the Mongolian race in which the

differentiation of inborn and acquired changes in pigmentation is often difficult, if not impossible. Future research in this connection should give additional information.

The ages of my patients ranged between 19 and 45 (19, 19, 26, 18, 45 and 25). Although the experience of the future and reports from other parts of China and the Far East will give further information regarding the particular age during which the disease is most often contracted, my opinion is that there is no limit in either direction, and that keratomalacia can be contracted at any age. The explanation of this is the fact that keratomalacia is not an actual disease of the eyes but, as in children, is merely one symptom of a general severe disturbance in nourishment which can be contracted at any age, and in which the eyes may participate. As to whether keratomalacia is confined to a special season or to special months, I can say only that all my cases occurred between March and July. It would seem, therefore, that there is a definite coincidence with epidemic xerosis and hemeralopia. Although the outbreak of keratomalacia in adults cannot be said to be due, as in children, to a greater demand of the body for vitamin A as a consequence of increased growing activity (Bloch [44] Blegvad,[24] and others), yet it occurs at a time of changed if not increased metabolism in the human being in the spring or in early summer when the heightened influence of the sun on the whole body seems to play its part.

Diet, however, is the deciding factor in the origin of keratomalacia in adults as it is in children. Each of my six cases came from the poorest classes and investigation proved that during the weeks preceding the disease of the eyes the diet of the patient was monotonous, consisting only of bread made from maize, a dish of millet with few additional substances, and "Tou Ya Tsai," a certain vegetable consumed throughout China. This vegetable is bean sprouts and contains no chlorophyl. None of these patients had eaten meat and green vegetables for weeks. At the same time the physical labor required was great. Butter is almost unknown to the poorest classes, and fresh fruit is not obtainable during the spring. Blegvad [24] summed up the reasons for disturbances produced by nourishment, in which vitamins were either absent or present only in small quantities, as follows:

(1) Insufficient consumption of fat-soluble vitamin A (*a*) through food which contains insufficient quantities of this ingredient and (*b*), through insufficient absorption of vitamin A in the intestinal tract (intestinal disease); and (2) increased need or consumption of vitamin A (*a*) during a period of rapid growth and (*b*) during severe illnesses.

44. Bloch: Klinische Untersuchungen über Dystrophie und Xerophthalmie bei jungen Kindern, Jahrb. f. Kinderh. **89**:405, 1919.

There is no doubt that in the majority of my cases, keratomalacia was caused by insufficient consumption of vitamin A, compared to which all other causes were of minor consequence.

H. Wu and D. Y. Wu [45] made the following statements about the nature of foodstuffs among the Chinese: "In North China wheat is the staple food, while millet, corn, rice and kaoliang are of secondary importance. In South China, rice is the most important cereal. In the class of legumes, soy bean and its products figure most prominently. About two-thirds of the fruits and vegetables are furnished by green vegetables, in which cabbage, leeks and onions take the lead, while the item fruits is filled mainly by melons of different kinds. Practically all the fats and oils are of vegetable origin; lard is the only animal fat used to any extent. Milk, butter and other dairy products are practically unknown to the average Chinese housewife. Contrary to the general belief, even eggs figure insignificantly in the Chinese diet." From this, it is apparent that the whole Chinese diet is not rich in vitamin A, since milk and all dairy products, from which occidentals get their supply of this vitamin, are absent in Chinese food. Spinach, which is very rich in vitamin A, is beyond the means of the poorest classes during the winter time. The Chinese cabbage is pale, almost without chlorophyl, and is therefore poor in vitamin A. Animal fat, as lard, plays no rôle in the kitchen of the people of the poorest class, among whom keratomalacia has been found. In addition to this, the vegetable oil is usually boiled for several days in the open air and in sunlight, a procedure which completely destroys the small quantity of vitamin A contained in these vegetable fats. It is therefore clear that the food of the poorest class is poor in vitamin A all year, but is practically devoid of it in the spring. The outbreak of xerosis epithelialis and keratomalacia in the spring, when the small reserve of vitamin A is exhausted, is easy to understand. There is one other circumstance of importance, i.e., the heavy physical labor, with the consequent increased consumption of all foodstuffs, including the vitamins. In addition it must be remembered that the people of both town and country are exposed for hours to the sun, which is hot in China during the months in question. This no doubt causes a considerable consumption not only of protein, but also of vitamins. We must not overlook the possibility that the "protein derivatives" which may have a poisonous effect on the body, perhaps produce in conjunction with insufficient and monotonous nourishment the local symptoms in the eye, as well as the general disturbance. If, in addition to these factors, intestinal and other debilitating diseases occur, further drain-

45. Wu, H., and Wu, D. Y.: Study of Dietaries in Peking, Chinese J. Physiol., 1928, no. 1, p. 135.

ing the reserves and interrupting the consumption of the necessary foodstuffs, the outbreak of keratomalacia will be hastened. It is well known that such debilitating diseases as syphilis, tuberculosis, dysentery, cholera, typhus, typhoid fever, etc., play an important rôle in precipitating keratomalacia in children. This is also true of keratomalacia in adults with whom, however, the disease may often have commenced through a self-imposed decrease or deliberately chosen monotony in food, perhaps forced on them by circumstances. In this connection the appearance of xerosis in adults after strict ritual fastings or when stationed in remote forts should be mentioned. I was unable to ascertain whether this applied to keratomalacia as well, as only abstracts of the literature were available, but keratomalacia appears after deliberate emaciation through monotonous and insufficient food (Schoeler[46]), and in teetotalers (Wikerkiewicz[21]). Two of my patients admitted that they had had diarrhea for a fortnight before admission, so that dysentery was suspected, but several carefully examined stools as well as a thorough medical examination gave no indication of dysentery or any other intestinal disease caused by bacteria or amebas. None of may cases revealed any signs of advanced tuberculosis, and in each the Wassermann reaction was negative. I think the reason why so much importance has been attached to intestinal disease as the direct cause for infantile and adult keratomalacia is the diarrhea which is frequently observed either shortly before the symptoms of the eye commence or during the course of the disease itself. It appears, however, that this diarrhea has its origin in a simultaneous degenerating disease of the mucous membrane of the intestines, similar to the diarrhea accompanying severe "Mehlnährschäden" (Cerny and Keller[47]) and general decomposition of new-born children or infants in the first year of life. In my experience this diarrhea is merely a concomitant symptom of keratomalacia, but is not the actual cause of the disease of the eye; it merely represents one symptom of a general disease caused by malnutrition.

GENERAL SYMPTOMS OF KERATOMALACIA IN ADULTS

In view of the foregoing observations, there is no doubt of the existence of a typical keratomalacia of adults which develops uninterruptedly as a continuation of advanced xerosis epithelialis. The local clinical symptoms have already been outlined, most points substantiated in several instances. On closer clinical examination, certain general symptoms are found which reappear in so regular and insistent a manner as to

46. Schoeler: Fälle von Bindehautxerose mit Hornhautgeschwüren bei gewaltsamen Entfettungskuren, Berl. klin. Wchnschr., 1887, no. 52.

47. Cerny and Keller: Die Ernährung des Kindes, Leipzig, 1906, p. 67.

indicate that keratomalacia is only one condition of a general disease, the symptoms of which, so far as I have been able to observe them, are now described briefly. There seems to be no doubt that the same symptoms exist in infantile keratomalacia, but they are less distinct, for they succeed each other far more rapidly and therefore much less clearly. In addition, children usually succumb to the general disease on account of diarrhea and bronchopneumonia before the symptoms become as distinct as in adults.

In his "Tropical Medicine," Elliot [37] drew attention to certain general symptoms in keratomalacia of children in addition to the poor general condition already mentioned by earlier authors. Referring to Herbert,[48] he mentioned changes in the mucous membrane of the mouth and larynx causing hoarseness, nasal catarrh, bronchitis, chronic diarrhea, epithelial cells in the urine and rise of temperature. Both he and Hsu [36] mentioned the decrease of hemoglobin in the blood, and Stephenson [49] stated that strumous children were most often affected by this disease. These authors, as well as Kirkpatrick and Wright,[38] mentioned the peculiar dry, earthy consistency of the skin and hair.

One typical symptom is the rise of temperature, which is practically never absent in keratomalacia of adults. Though occasionally mentioned as one of the symptoms of the disease in children, it is often considered of no importance, but simply as accompanying the diarrhea or bronchitis or as a forerunner of the final bronchopneumonia. De Gouvêa,[11] who was the first to comment on the rise of temperature, attributed it to a disturbance of the general nervous system. Hsu [36] valued it as a typical symptom of keratomalacia of children, and mentioned it in practically every one of his ten cases, which occurred in children up to the age of 10. In adult keratomalacia, I consider a temperature of from 37 to 38 C. (from 98.6 to 100.2 F.) characteristic; it persists until the disease of the eye and the other general symptoms have taken a decided turn for the better, but it may considerably outlast this period, especially in cases of long standing. It should be emphasized that my first three patients, although suffering only from xerosis of the conjunctiva and cornea without keratomalacia, all showed also a rise of temperature. This was therefore not due to any ulceration of the cornea or any serious secondary infection of the interior of the eye such as abscess of the vitreous body or panophthalmitis. In severe cases, however, there is a considerable increase in temperature, rising almost to 40 C. (104 F.) and running an irregular and remittent course (case 3). With all these cases I made a special point of having the department of medicine search for any other possible cause of the

48. Herbert: Indian M. Gaz., 1897, p. 130.

49. Stephenson, S.: On Cases of Nightblindness with Peculiar Conjunctival Changes in Children, Ophthalmoscope **10**:14, 1912.

temperature, but no other reason was ever found. The possibility of acute or chronic infections of the intestines was eliminated by frequently repeated stool cultures; and of syphilis and tuberculosis, by the corresponding serologic tests.

The blood showed characteristic changes in a decrease of hemoglobin (Hsu [36] and others), although the red blood cells were practically normal. This appeared to be typical from the two severest keratomalacia cases with the greatest number of definite general symptoms, in which the hemoglobin was reduced to 65 per cent, whereas in the four milder cases it remained between 70 and 85 per cent. The results of the examination of the blood are shown in the accompanying table.

The table shows that the number of white blood cells is considerably above normal in the two worst cases (25,000 and 18,000 white blood cells, respectively) and that there were 90 per cent polymorphonuclear leukocytes, whereas the distribution in the remaining cases is approximately normal. In case 4, 7 per cent transitional forms were found.

Results of Examination of the Blood

Case	Red Blood Cells	White Blood Cells	Polymorphonuclears, per Cent	Lymphocytes, per Cent	Transitional Forms, per Cent	Hemoglobin, per Cent
1	4,600,000	7,000	80	20	—	75
2	4,800,000	8,200	78	20	2	85
3	4,600,000	10,000	72	28	—	70
4	4,300,000	5,800	64	28	7	80
5	3,800,000	25,000	90	10	—	65
6	4,800,000	18,000	90	10	—	65

On the whole, there is a mild oligochromemia in keratomalacia of adults, also an increase of polymorphonuclear leukocytes, which keeps pace with the general symptoms, at the expense of the lymphocytes. In this matter, however, further systematic examinations of the blood and study of blood curves are necessary.

The skin, apart from the eye, undergoes the most extensive and marked change of all. Its color ranges from a peculiar faded gray to grayish yellow and is described in the literature on one occasion as "subicteric." I am not in a position to ascertain clinically if these changes in color are due to an increase of the melanin of the chromatophores of the skin, as in the conjunctiva. This will have to be left to future histologic examinations of skin sections, as mistakes are easily made in dealing with the yellow races. It is still an open question if deposit of bile in the skin takes place in severe cases, in which diseases of the liver are not improbable. This would constitute a connection with keratitis hepatica observed by earlier authors (Weiss,[2] Hori,[3] and others). Examinations of the liver, and the liver function test with phenoltetrachlorphthalein made by the medical department in cases 2 and 3 gave negative results. These tests only concern the two mildest

cases and in spite of the negative findings I consider it by no means impossible that changes of the liver as a part of the whole disease, may occur in severe cases. In the severe cases (cases 4, 5 and 6) these examinations were unfortunately omitted because I myself did not realize clearly enough the possible connection. Studies in this direction are already going on. A further striking sign is the condition of the surface of the skin which is somewhat rough, dry and earthy to the touch in practically all cases, including those of corneal xerosis and even in prolonged cases of conjunctival xerosis not mentioned in this paper. In severe cases one has the impression of the entire skin having been dusted with coarse powder. In some cases there is decided scaling. In case 5 this occurred to such an extent that the bed was always full of scales (hyperkeratosis). This roughness was due not only to the lack of sebum but also to a long adherence of an excessive number of horny cells on the surface of the skin (parakeratosis).

The skin is usually slack and heavily lined with folds, or covered with minute wrinkles, especially near the joints and on the face, so that the patients appear far older than they are. This condition of the skin is especially noticeable in very advanced cases, while younger patients, in the first stages, develop an edematous swelling and puffiness of the skin especially of the face and of the lids. The patient in case 5 had definite edema of the legs which could be attributed neither to the kidneys nor to the cardiac condition. To what extent a stowing of the lymph and changes of the blood vessels are responsible for this non-inflammatory edema, is a matter for future clinical and histologic investigation. The discoloration of the skin may be influenced in part by the presence of lymph fluid or of other cell-like elements in the subcutaneous tissue.

The inactivity of the sebaceous and sweat glands is conspicuous. The lack of sebum is responsible not only for the dry, earthy feeling of the skin, but also for the hundreds of comedones which, in four of my cases, covered the skin of the face and part of the chest and neck. These comedones showed that the sebaceous glands had ceased to act, and that the sebum which they were unable to discharge through the ducts, was being oxidized on the surface by air. Often a secondary infection of the comedones and the hair follicles takes place, thus showing multiple small follicular abscesses all over the face similar to a simple acne. These disappear as soon as the general condition improves. It has not been ascertained by histologic examination if the sweat glands take part in the process, but judging by the constant dry state of the skin it is probable that they do. It is not improbable that the peculiar consistency and changes of the whole integumentum contribute to a disturbance of the "Waermehaushalt" of the body and account partly for the rise of temperature which is present in almost every case. The changes of the

skin are not stationary, but develop according to the degree of the whole condition, like the changes in the eye. Cracks appear in the earthy wrinkled skin, and bacteria which wander into the hair follicles cause secondary mild furuncles or follicular abscesses. The inflammatory nature of these is recognized by the reddened area. There are also sometimes large hollows in the skin, at times undetermined to a depth of 2 cm. Although these abscesses show a considerable amount of discharge, the slight redness of the edges is due rather to maceration by the secretion than to a real inflammatory condition. Practically no inflammation is present anywhere in spite of the severity of the condition. A picture of dissolution, a decay of the external skin which I would like to name "dermomalacie," in accordance with the clinical and anatomic condition of the cornea, should be regarded as entirely separate from the formation of inflammatory abscesses. Although in these abscess hollows vast quantities of saprophytic and pathogenic germs are found which may further help to dissolve the tissue, it is probable that they are of no greater importance than pneumococci and streptococci are to the cornea in infantile keratomalacia as well as in keratomalacia of adults. They grow in vast quantities on the necrotic tissue without being in any way connected with the original cause of the disease. The skin in keratomalacia of adults is also merely the culture medium for the germs, which rapidly predominate as a consequence of the changed condition of the epithelial cells, the whole metabolism of the body and the lack of any power of resistance. In case 5, I counted more than thirty decayed hollows of the skin, and in case 6 there were also several abscesses of this kind. In cases in which nourishment rich in vitamin A is given, these abscesses and the deepest pockets dry up in a wonderfully short time without any surgical treatment. It is remarkable that the decayed regions are painless, a further proof that they have no inflammatory cause.

In every one of my cases the hair was also extremely dry, and in the more advanced cases it became wiry. The scalp was covered with dandruff; the hair easily fell out and turned gray. Special examination in this direction may possibly reveal characteristic histologic changes of the hair itself. Similar changes of the hairs are well known from experimental vitaminose in rats.

I was able to observe a curious change in the nails which no doubt is also one of the conditions of degeneration. In case 5, the worst as regards the number of general symptoms, the nails were seamed with furrows which ran lengthwise and peeled off at the surface in small particles. The outer margin was slightly jagged and irregular, but the whiteness around the whole nail, as if the cuticle had spread practically all around, was most striking of all. The nail itself was dull, horny and not as transparent as when normal, so that no pink blood color was

visible through it. In spite of the patient's premature discharge from the hospital, these symptoms were well on the return to normal after thirteen days of nutritious diet.

There are indications that other mucous membranes of the body than those of the eye are affected by this disease. Only further histologic investigation can determine whether these changes occur on the same pathologic anatomic lines as in the eye, i. e., a transformation of cylinder epithelium to the squamous epithelium, and of squamous epithelium of the mucous membrane to epithelium of the skin with parakeratosis and hyperkeratosis. The dryness of the mouth, combined with the bluish coloring of the mucous membranes of the mouth and throat frequently seen, also the hoarseness (Herbert [48]), could be caused by a similar change of the mucous membranes of the mouth, throat and pharynx. Indeed it is not improbable that the frequently mentioned bronchitis of children, which at times accompanies the whole course of the disease, and even the final bronchopneumonia so often observed in children as sometimes in adults (Blegvad [24]) may originate in analogous changes of the respiratory epithelium, so that first the epithelium of the bronchi may lose its normal structure, and finally the epithelium of the lung alveoli may forfeit its respiratory character and become unfitted for the inhaling and exhaling of gases. This hypothesis would explain the bronchopneumonia as the typical final disease and the typical form of death in keratomalacia. These impressions can be recorded only with the greatest caution and with the reservation that careful histologic and clinical investigations of characteristic cases, now apparently occurring only in the Far East, should verify the correctness of these suppositions.

The extent to which the other mucous membranes of the body, especially those of the intestinal and genito-urinary tract, participate in this disease, as certain symptoms seem to indicate, can only be mentioned in passing, on account of the lack of sufficient and reliable material. During the keratomalacia, five of six of my patients had severe diarrhea, which did not have the significance of the debilitating causative factor for keratomalacia. Only in case 2 was the patient supposed to have had an attack of dysentery some time before. The diarrhea, in fact, in these five cases only occurred shortly before admission to the hospital or developed later during observation. One is, however, by no means justified in alluding to an intestinal disease as resulting in keratomalacia, even though intestinal symptoms appear before the onset of the symptoms of the eye. Perhaps in the future we may succeed in tracing back many unexplained forms of diarrhea even in adults, to a degenerative pathologic anatomic condition of the mucous membrane of the intestines. At this point, a connection is made with that vast group of diseases of early infancy due to faulty and insufficient nourishment coinciding with intestinal catarrh, in which

pathologic anatomic studies at an early stage have shown the mucous membrane of the intestinal tract in a state of high grade atrophy. As it is a well known fact that keratomalacia occasionally develops with essential atrophy of the intestinal tract (Fehr [50]), there is no mistake in placing the diarrhea, so frequently observed in cases of keratomalacia in adults, in this pathologic anatomic category. One is thereby enabled to understand how it is that this diarrhea, as a coordinate symptom of keratomalacia, either precedes the disease or develops simultaneously with it. The importance of this diarrhea, i.e., of the intestinal disease, remains, as it is probably the intestines that are first affected by the general disease caused by insufficient and poor nourishment, without the disclosure of any striking clinical symptoms.

The interesting part of the whole question lies in the fact that apparently degenerative intestinal catarrhs of this kind may also occur in adults. The presence of severe constipation, as remarked in case 5, can easily be understood under the circumstances. Unsuccessful attempts were made in all cases to clear up the etiology of the diarrhea by thorough medical examinations, prolonged study of the patient and repeated bacteriologic examinations of the stool. Also in the one patient who gave a history of dysentery two years before, no indication of an infectious disease of the intestines could be found, in spite of repeated examinations of the stool. It is also remarkable that the diarrhea generally vanished within a week in spite of the diet prescribed which is certainly not qualified to cure a diarrhea due to infectious intestinal diseases, consisting as it does of cod liver oil, butter, fat, milk and fruit. The intestinal symptoms were, in fact, among the first to disappear. This is remarkable and suggests the need of care in the diagnosis of such diarrhea as occurs in dysentery and typhoid. It must be admitted, however, that severe diarrhea immediately precedes the development of the corneal disease, and in advanced cases, especially in children, can prove a "signum mali ominis." Future bacteriologic, chemical and especially morphologic examinations of the stool for the presence of formed elements of an excessive quantity of discarded epithelium and for the condition of the exfoliated epithelium cells, and histologic examinations of the larger parts of the intestinal tract during autopsy will give much information and are absolutely necessary to clear up the whole question. This statement does not question the fact to which special reference has been made in the first part of this paper, that severe infectious intestinal diseases, such as typhoid and dysentery, may act as an exhaustive factor and lead indirectly to the outbreak of keratomalacia of adults as they do in children.

50. Fehr: Lehrbuch der Kinderkrankheiten, ed. 6, 1920, p. 240.

To what extent the observation of a nongonorrheal secretion discharging in small quantities from the urethra in case 6 during the acute stage of the disease, would justify the assumption that the epithelium of the genito-urinary tract is also affected, remains to be proved by further examination.

As mentioned before, the sweat glands and the sebaceous glands participate to a large extent in the form of hypofunction and afunction. Many authors both early and recent have remarked also on the fact that the secretion of the lacrimal gland is either diminished or entirely lacking in cases of keratomalacia of children. It is hard to say at the present time whether the larger glands of the body, such as the liver and kidneys, and the glands of internal secretion participate in the whole process. The keratomalacia accompanying diseases of the liver, described especially in earlier papers (Elschnig and others), certainly would suggest this, as would also the subicteric discoloration of the skin, observed occasionally in children with keratomalacia; and whether the swelling of the lymph glands of the neck in Hsu's case 8 and in my case 6 indicates participation of the lymph glands in keratomalacia, or is to be traced to other causes, such as as a flaring up of an old tuberculous process. Wright [38] believed that also the thyroid gland is affected in keratomalacia. In this connection, it is interesting to find that McCarrison [51] in an experimental paper on edema in rats fed on food containing practically no vitamins, pointed out that all glands of internal secretion became atrophic with the exception of the suprarenal and the pituitary glands. Okamoto [52] mentioned the same condition in rabbits. Without entering into further particulars with regard to the vast literature on experimental avitaminosis, and while taking into consideration the fact that the results gained by experiments on animals can only rarely be applied fully to the human body, in my paper based mainly on clinical observations I will not omit to mention the work of Wolbach, Burt and Howe [53] who, in examining white rats with xerophthalmos, found that widely differentiated cells with secretory capacity lose their functional ability and are converted into the type of nonsecretory epithelium. This occurs in the entire upper respiratory tract, the salivary glands, the pancreas, the pelvis of kidney, the bladder, the seminal vesicles, the epididymus and the prostate.

SUMMARY AND CONCLUSIONS

In reconsidering which parts of the eye are affected by keratomalacia and how this disease manifests itself in the various parts of the human

---

51. McCarrison: Deficiency Disease, with Special Reference to Gastro-Intestinal Disorders, Brit. Med. J. **1**:820, 1920.

52. Okamoto, K.: Studies on Experimental Xerophthalmia, Japan Med. World **5**:180, 1925.

53. Wolbach, Burt and Howe: Tissue Changes Following Deprivation of Fat Soluble A Vitamin, J. Exper. Med. **42**:753, 1925.

body, it is found: (1) that it is primarily a disease of the "integumentum commune" with its appendages, the skin glands, hair and nails; (2) that the epithelium cells of the respiratory and digestive tract appear to be affected, and (3) that certain other organs of a glandular type, i.e., of ectodermal origin, such as the lacrimal gland, the sweat and sebaceous glands, probably the liver, and the kidney, may change. The extent to which the glands of internal secretion are concerned is unknown and will have to be investigated thoroughly. The pigmentations, which appear in such a characteristic way on the external skin and on the conjunctiva of the eye, indicate that there is probably a disease of the suprarenal gland similar to that in morbus Addisonii. We are dealing, therefore, with extensive "system disease" in the broadest sense of the word, a disease of the greater part of the ectodermal leaf of the body, and is caused by undernourishment and by the absence of certain food elements, namely, vitamin A. In its mildest forms, this avitaminose occurs in the eye as xerosis of the bulbar conjunctiva, and culminates in its severest form in keratomalacia with total blindness, and when accompanied by bronchopneumonia, in death. The aim of future research work should be to disclose the nature of the initial stages of the general symptoms herein indicated which probably may be studied in the mildest forms of this disease, such as in xerosis epithelialis with hemeralopia which is commonly found in Europe and America.

In view of the statements in the first part of this paper, no further evidence is required that the condition in the eye is a disease of ectodermal elements; this is proved by the disease of the conjunctiva and corneal epithelium, the change of the former to a type of epidermis, the pigmentation of the basal cell layer, and the disease of the shagreen of the lens. Finally, hemeralopia is only an expression of the disease of the epithelial elements, the rods and cones, and of the pigment epithelium of the retina.

OCULOGLANDULAR FORM OF TULAREMIA*

DERRICK T. VAIL, JR., M.D.
CINCINNATI

The disease known as tularemia needs no introduction. It has occupied a great deal of attention in the literature, especially during the past four years. For the widespread knowledge concerning the disease, great credit is due to Edward Francis, surgeon of the Hygienic Laboratory, U. S. Public Health Service, Washington, D. C., although the actual discovery of the disease in man, the isolation of the causative germ and its verification were all matters of record in the literature at least five years before he began his investigations. The general phase of this subject is beyond the scope of the present paper, since it is mostly concerned with the ocular type of the disease. Certain features of the early history, however, should be accentuated since the credit for the discovery of the human type of the infection is entirely due to ophthalmology.

HISTORY

In 1908, William B. Wherry, bacteriologist, was assigned to the Port of San Francisco to investigate plague among ground squirrels.

In 1910, George W. McCoy, connected with the U. S. Public Health Service, found that he was unable to isolate *Bacillus pestis* from a certain number of infected squirrels brought to his laboratory, although the pathologic condition of the diseased squirrels was identical with that of subjects with bubonic plague. There was a laboratory rule that there must be a positive culture in all cases of plague before a definite diagnosis was made.

In 1911, McCoy and Chapin, working on this plaguelike disease in the ground squirrel, identified an organism almost through chance which they named *Bacillus tularense* after the county of Tulare in California, in which the disease was first observed. In attempting to isolate this organism, they used every possible culture medium that they knew.

They had on hand some culture tubes containing egg yolk mediums for the isolation of the tubercle bacillus. As a last resort they inoculated these with infected material, and much to their satisfaction they found that the organism (*B. tularense*) would grow. They also discovered that certain animals, especially rodents, were highly susceptible to inoculation with the organism, which produced the same type of disease they

* Submitted for publication, June 24, 1929.

* Read by invitation before the Eye, Ear, Nose and Throat Section, Illinois Medical Society, Peoria, Ill., May 22, 1929.

observed among the ground squirrels. At that time, they prophesied as follows:

"We do not know whether the organism causing this disease is pathogenic for man, but judging from the large number of species that are susceptible, we are inclined to suspect that man might contract the infection."

In 1912, they worked out an agglutination test which has been extremely useful in proving the presence of this disease. At that time, the discovery of the organism did not create any particular general interest. In the fall of 1913, however, a patient consulted my father, Dr. D. T. Vail, Sr., for a severe and unusual form of conjunctivitis of the left eye. Recognizing that this was something he had neither seen nor read about, my father sent the patient to Dr. Wherry, who was then professor of bacteriology at the University of Cincinnati, for a bacteriologic examination. This proved to be the first case on record of tularemia in man which was diagnosed and proved by laboratory methods.

Wherry and Lamb worked on this case for several months, exhausting every possible method of cultivation but keeping the disease going through laboratory animals. Wherry had been familiar with McCoy and Chapin's discovery, although it did not occur to him until several weeks had passed that this was a human case of the disease that had been described among the ground squirrels. When he did think about this condition, the clinical problem was solved immediately, and he succeeded in isolating *Bacillus tularense* in pure culture. Among other experiments, he dropped an emulsion from a culture into the healthy eye of a guinea-pig and reproduced the conjunctival disease, with death of the animal in four days.

This is an extremely important observation, since it indicates that the conjunctiva does not need to be traumatized for the organism to penetrate and accounts for the extreme ease with which tularemia conjunctivitis is caught.

In 1914, Wherry and Lamb found two rabbits in Indiana infected with the disease and appealed to physicians to be on the lookout for a condition of this sort and to send in material from obscure cases. Their appeal was unheeded, and it was not until much later that the general profession became interested in tularemia.

In 1907, Ancil Martin, an ophthalmologist of Phoenix, Ariz., in a letter to Professor Novy of the University of Michigan described three cases of conjunctivitis which he had seen in his practice and to which he gave the name of "rabbit septicemia." In one of these cases, the condition has since been proved by agglutination (1925) to be tularemia. The letter, however, was pigeonholed, and nothing further came of it until after Francis' work in 1919.

In 1911, Pearse, in Utah, under the title of "Insect Bites," described six human cases of the disease which at that time was known as deer-fly fever.

In 1919 and 1920, Francis investigated deer-fly fever, recognizing the identity of this disease, and named it tularemia. He isolated the organism and with Mayne demonstrated the agency of the deer-fly in transmission.

In 1924, Parker and Spencer, in Montana, reported the agency of ticks in the maintenance and transmission of the infection. They demonstrated hereditary transmission through the egg of ticks.

In 1925, O'Hara described a disease in Japan which was contracted while dressing wild hares. This was proved by Francis and Moore to be tularemia.

In 1928, certain Russian authors reported a series of 105 cases of a plaguelike disease occurring in the Ural Valley, Russia, in people who had been hunting and skinning water rats (vole). In this series, two cases were found to be of the oculoglandular type. These authors suspected that the disease was tularemia and they sent material to the U. S. Public Health Service for confirmation.

Professor Zarhi of Sverdlovsk (Ekaterinburg) in the province of Perm, Russia, sent material from a human case to Dr. McCoy, which the latter proved to be tularemia.

The distribution of tularemia, therefore, is widespread throughout the United States; it has been found in Japan and recently in Russia.

At the risk of being called chauvinistic, I should like to point with pride to the part Cincinnati played in the discovery of this peculiar disease. The first human case was discovered in Cincinnati and was proved by the bacteriologic department of the University of Cincinnati. The first three cases were described by Cincinnati ophthalmologists, Vail, Sattler and Lamb, members of the faculty of the University of Cincinnati Medical School, and Francis obtained his medical training in Cincinnati. As far as I know, it is the only widespread disease affecting the human body which has been discovered primarily through the agency of ophthalmology.

Those who are further interested in the general features of this subject are referred to a recent paper by Edward Francis, entitled "Summary of Present Knowledge of Tularemia," and also to "Tularemia," by Walter Simpson (New York, Paul B. Hoeber, 1929).

SUMMARY OF OPHTHALMIC CASES

Through the courtesy of Dr. Edward Francis, I was supplied with the names and references to those observers throughout the country who had reported proved cases of tularemia conjunctivitis. The following is a summary of the important features of these cases.

There are thirty-five undoubted cases of tularemia conjunctivitis and one doubtful case, that of A. C. Barry. This patient had general tularemia, but the conjunctivitis was mild and bilateral and cleared up quickly after the use of 10 per cent protargin mild solution.

The right eye was affected in twelve cases, the left in nineteen and both eyes, in four.

The age of the youngest patient was 7 years and of the oldest, 72. Thirty-one males were affected and four females.

The cases were distributed throughout the United States; there were eight cases from Montana and three from Wyoming. The occupations of the persons affected were: farmers, twenty-five (this includes wives and children); meat cutter, one; cook, one; students, two; sheepman, one; rancher, one; bookkeeper, one; laborer, one, and unspecified, two.

The sources of infection were as follows: handling or skinning rabbits (wild or jack), twenty-three cases; crushing a tick, eight cases; portion of a crushed fly, one case; bile from an infected woodchuck, one (Simpson, in a personal communication), and no history of infection from an animal, two cases.

Those who handled ticks generally crushed them between their fingers, the infected juice flying into the eye.

One patient had the habit of rubbing an eye which was affected by congenital stenosis of the lacrimal duct. She did this while cleaning infected rabbits, introducing the virus into that eye.

While a farmer was removing ticks from a horse, a foreign body struck his eye, and he rubbed it with infected fingers.

While cleaning rabbits, one farmer was struck in the eye by a flying piece of rabbit meat.

Two patients were bitten on the cheek—one by a fly, the other by a tick—and each slapped at the insect, crushing it. The infected material entered the eye.

While eviscerating a woodchuck, a farmer ruptured its gallbladder, and the infected bile struck him in the right eye (Simpson).

Those who handled infected rabbits undoubtedly introduced the infective material into the eye by their fingers.

The following types of lesions were found: small yellow ulcers, seventeen cases; papules or nodules, three cases; boggy or thickened conjunctiva, five cases; iritis, two cases, and corneal involvement with perforation, one case (Magath and Yater).

All but three patients mentioned intense swelling of the lid and thick, edematous and redundant conjunctivae. The size of the ulcers varied from 2 to 6.0 mm. The number of ulcers present ranged from one to ten; the average number was six.

More of the lesions were situated on the conjunctiva of the lower lid, usually in the tarsal area. Three cases showed lesions on the bulbar conjunctiva (those of Vail, Jr., Clark, and Pfunder). One case (Junkin) showed a papular rash on the head and shoulders on the fourteenth day of the disease, one papule at the inner canthus causing intense edema of the lids.

The glands involved were: preauricular, twenty-three cases; cervical, sixteen cases; parotid, seventeen cases, and submaxillary, twenty-six cases. Many of these glands suppurated and had to be incised.

Three observers reported that the glandular involvement appeared one, three and four days, respectively, after the symptoms in the eyes. The rest of the cases showed simultaneous glandular involvement.

In regard to the general reaction and duration of the ocular symptoms, all but two patients had a general reaction with a high temperature, from 103 to 104 F. One patient was able to continue his work after a few days. One patient had no elevation of temperature at any time (Jackson). The febrile reaction lasted from one to six weeks, the average four weeks. The temperature was of the typhoid type. The conjunctivitis lasted from ten days to two months, the average time being four weeks. The majority of patients were incapacitated for from five to six months.

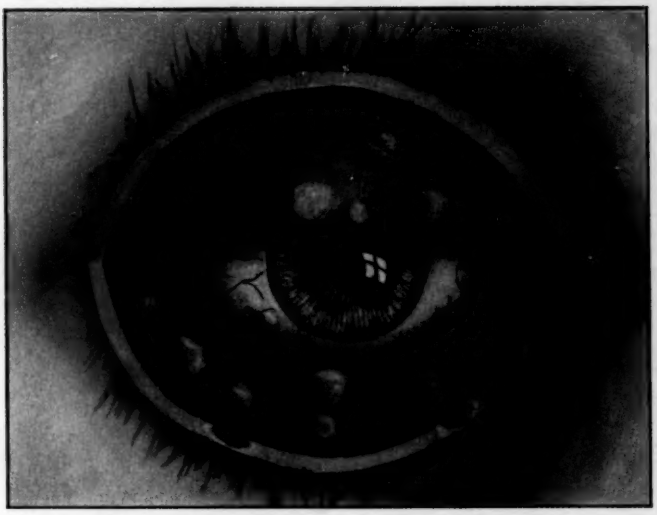
The following types of discharge were found: slight mucoid, or mucowatery, nine cases; purulent, two cases; mucopurulent, four cases; profuse (type not mentioned), one case, and none, one case.

In all cases except one, the condition was verified by inoculation into guinea-pigs or by agglutination, one (that of Martin) eighteen years later.

The one unproved case which is included is that reported under "Parinaud's Conjunctivitis," by T. E. Fuller. This case is so typical from the history of infection by a crushed tick to its clinical signs of incubation period, high fever, conjunctival ulcers and glandular involvement, that there is no doubt in my mind that it is a true case.

DESCRIPTION OF THE TYPICAL OCULOGLANDULAR FORM OF THE CONDITION

After a prodromal period, anywhere from twenty-four hours to ten days (the average being three and one-half days), the eyelids begin to swell and itch, and at the same time the patient has severe headache, chills and fever and vomits. The onset is sudden; almost simultaneous with the swelling and edema of the lids, the glands of the head and neck on the affected side, namely, the preauricular, parotid, submaxillary and cervical, become enormously swollen and tender. If the patient is seen shortly after the acute onset, the ophthalmologist will find scattered throughout the conjunctivae of the everted lid, small yellow discrete



Tularensis conjunctivitis.

ulcers, deeply situated in the chemotic conjunctiva, which is a vivid scarlet. Dr. Vail, Sr., picturesquely said, "They look like yellow polka dots in a piece of turkey red calico." As a general rule, the cornea is not involved and the bulbar conjunctiva is not invaded. In two cases, however, single ulcers have been described in the bulbar conjunctiva, and in one case nodules were found. There is a scanty mucowatery discharge, generally straw-colored, which is sufficient to glue the lashes together.

The patient is obviously ill and complains of pain in the eye. As the course of the disease progresses, the ulcers tend to become nodular and covered by a thin membrane. This may be found at any time after the seventeenth day of the disease. The active conjunctivitis continues for about five weeks, when the swelling gradually recedes and the nodules disappear without leaving a scar. Several months later, one can often find a thickened and congested conjunctiva in the retrotarsal folds. The condition of the glands, on the other hand, persists for many months and may progress to suppuration. The patient is usually incapacitated for six months or longer.

Smears and cultures of the conjunctival sac, taken any time during the course, are always reported negative except for a few secondary invaders, such as the xerosis bacillus, or the staphylococcus or streptococcus. One cannot succeed in growing the culture on egg yolk medium by direct inoculation. After an emulsion is made from the conjunctival scrapings and injected into the peritoneum of a guinea-pig, the animal will die within from five to seven days from septicemia. Autopsy reveals the presence of minute yellow dots scattered throughout the liver and spleen. The lymph nodes are enlarged and hard. Cultures taken from the foci in the spleen or liver will readily grow on egg yolk mediums.

There has been a mortality of 24 of 654 reported cases of all types. Three of the 34 cases in which the eye was affected have resulted in death.

BACTERIOLOGY *

Bacterium tularense is a small, pleomorphic organism, gram-negative, nonmotile and nonspore-bearing. It grows only under aerobic conditions. Its optimum temperature is 37 C., and its optimum p_H range is between 6.8 and 7.3. It ferments dextrose, levulose, mannose and glycerin, forming acid but not gas. It grows well on coagulated egg yolk and blood-dextrose-cystine-agar, but not on ordinary laboratory mediums such as plain agar, plain bouillon, gelatin, potato and milk. Bacillary, coccidial and bipolar forms are noted. In smears, it stains well with crystal violet or aniline gentian violet, and in sections it stains best with Giemsa solution. In three of eight

* From Francis' "Summary of Present Knowledge of Tularemia."

attempts, it passed through Berkefeld filters which held back a small staphylococcus.

Heat.—A temperature of from 56 to 58 C. kills the organism in cultures and in spleen tissues in ten minutes. Thorough cooking renders infected tissue harmless.

Solution of Formaldehyde.—Cultures suspended in saline solution containing 0.1 per cent of solution of formaldehyde (37 per cent strength) are rendered nonvirulent after twenty-four hours.

Tricresol.—Spleen tissue rubbed up 1 per cent tricresol was free from infection after two minutes.

Glycerin.—Pure undiluted glycerin into which cultures or spleen tissue are placed preserves the virulence for one month at room temperature for six months at 10 C., and for one years at —14 C. Glycerination in conjunction with annual or semiannual animal passage serves to perpetuate the virulence of a strain for years.

Freezing.—Spleen tissue frozen at —14 C. lose its virulence in one month. Frozen rabbits are infective for three, but not for four, weeks.

Drying.—The virus resisted drying in bedbug feces for twenty-six days.

Agglutination.—1. There was a complete absence of agglutinins for tularense in the first week of illness.

2. Specific agglutinins were always present at some time in the second week.

3. There was an abrupt rise in the agglutination titer in the third week.

4. A fall of titer began in the eighth week.

5. A gradual diminution in the amount of agglutinin took place until the end of the first year; the average titer of 21 cases was 1 : 140.

6. Specific agglutinins remained for years in blood of long recovered cases and did not disappear from any case, even 10, 11, 12, 15, 18, 19 or 24 years after recovery.

Susceptibility.—(1) High susceptibility in man, monkey, ground squirrel, rabbit, guinea-pig, mice, woodchuck, opossum, young coyotes, pocket gopher, porcupine and chipmunk.

(2) Slight susceptibilty in rats, cats, sheep and goats.

(3) Nonsusceptibility in horse, cattle, hog, dog, fox, chicken and pigeon.

Transmission Among Animals.—Blood-sucking insects, lice, flies and ticks, are believed to transmit the infection from rabbit to rabbit in nature, thus contributing to the maintenance of infection throughout all the months of the year and perennially.

Seasonal Incidence.—Ticks (March to August) and flies (June to September) have a seasonal prevalence and rabbits are protected by law, except in certain months (November to February).

OCULAR PATHOLOGY

Microscopic studies of the conjunctival lesions have not been made. Vail, Sr., said that the solitary lymph nodes of the conjunctiva are affected and the ulcers which extend through to the tarsus are punched out and filled with necrotic yellow plugs. Sattler excised a small nodule from the bulbar conjunctiva which appeared five weeks after the onset of the conjunctivitis, with immediate exacerbation of the local and general condition, lasting two weeks. Histologic examination showed a granuloma but no giant cell, and portions of this node did not produce the disease on injection into a guinea-pig. In one case conjunctival scrapings taken on the twenty-first day did not produce the disease in a guinea-pig (Vail, Jr.). The general pathology need not concern us here. It has been well gone into (Wooley, Simpson) and described. Briefly, there are areas of focal necrosis scattered throughout the spleen, liver and lymph nodes.

DIAGNOSIS

1. *Parinaud's Conjunctivitis.*—This disease might be called the *bête noire* of ophthalmology. A study of the literature reveals innumerable cases, few of which can be definitely grouped. It appears that any kind of unilateral conjunctivitis with regional lymphadenitis has been called "Parinaud's" by the observer, and in the majority of cases, few or no attempts have been made to run the etiologic factor to earth.

Perhaps it would not be out of place to return to Parinaud's original description (Morax: French Encyclopedia, vol. 5, p. 774).

> The affection is ordinarily monocular. It resembles at first glance a granular conjunctivitis. The conjunctiva is the seat of red or yellow vegetations, semi-transparent at the beginning, opaque at a later stage, which can reach the size of a large pinhead. Alongside of these fleshy granulations, one finds very minute ones entirely yellow, which at first made me think of tuberculosis of the conjunctiva. In one case these granulations were limited to the tarsal conjunctiva of the upper lid. In two other cases they occupied the two lids, the culdesac and a part of the bulbar conjunctiva. The cornea does not appear to have any tendency to be involved.
>
> There is a mucous secretion with very dense fibrinous deposits but no actual suppuration.
>
> The lids are swollen, firm to the touch, with nodules which makes one think of chalazia.
>
> The parotid region becomes very rapidly the seat of an inflammatory swelling which can extend to the neck and in the midst of which one discovers swollen and sometimes softened glands.
>
> There is fever with irregular chills; it can persist for a very long time, but always remains moderate and does not gravely react on the general state.

The swelling of the parotid deminishes toward the fifth week but the glandular enlargement persists. Some disappear by absorption, others suppurate. The evolution of the abscesses is very slow.

For convenience, therefore, one can follow the outline suggested by S. Gifford and submit the following groups:

A. Leptothrix Conjunctivitis (Verhoeff): In 1913, Verhoeff discovered a leptothrix in case clinically diagnosed as Parinaud's conjunctivitis. Since then, he has analyzed eighteen cases in his experience, in seventeen of which he found the leptothrix. Of all the clinical forms, this comes most near to Parinaud's original description. Verhoeff's description follows:

Parinaud's conjunctivitis, or leptothricosis conjunctivae, is a subacute inflammatory condition of the conjunctiva due to infection with a minute leptothrix, and is always associated with inflammatory enlargement of the preauricular or other regional lymph glands. The source of infection is unknown. In some cases there is a history of slight trauma to the conjunctiva preceding the infection. The incubation period is from three to seven days. The glandular enlargement is synchronous with the onset of the ocular symptoms. The essential conjunctival lesions consist of focal areas situated immediately beneath the epithelium, infiltrated with endothelial phagocytes in various stages of necrosis. Clinically, these foci appear as opaque grayish areas from about 0.5 mm. to 4 mm. in diameter. In individual cases they may be single or multiple, and may occur in any part of the conjunctiva including the bulbar portion. They contain the leptothrices in great numbers. Beneath these areas more or less granulation tissue is produced which may cause the conjunctiva to project in the form of polypoid nodules. The latter occur chiefly on the fornices. Ulceration seldom if ever occurs. In the affected regions, the conjunctival tissue is congested, edematous and densely infiltrated with chronic inflammatory cells, among which plasma cells largely predominate. In marked cases this causes the fornix to become everted and to project like a curtain over the cornea. Frequently the normal conjunctival lymph follicles are greatly enlarged. The congestion and edema extend through the whole of the lids so that in severe cases ptosis may result. The conjunctival secretion is slight in amount and mucopurulent in character. The cornea is unaffected. The local subjective symptoms are not severe, and constitutional symptoms are slight or entirely wanting. The affected glands seldom break down.

The disease is almost if not always unilateral, attacks almost exclusively children and young adults, and males more frequently than females. It is most prevalent in winter, and so far as known, is never transmitted from one individual to another. The most efficient treatment is excision of the gray areas and nodules. The duration of the eye symptoms after this treatment is from one to five weeks. The glandular enlargement may persist for a considerably longer period.

Leptothrix has been found in similar cases by Keiper, Lemoine, Dunphy, Dean, Wherry and Ray, and Gifford. This establishes the unity of this disease fairly well, and because of its marked resemblance to Parinaud's original description deserves first place. S. R. Gifford, in describing three cases, mentioned eosinophilia and expressed the belief that this may play some part in the differentiation of this disease.

B. Tuberculosis of the Conjunctiva: Several cases have been reported, the clinical signs of which closely simulate tularemia except in its most typical form (Tomassene and Bartos and Motto). The chief point in differentiation lies in the gradual onset in tuberculosis. This sign, however, is not necessarily to be trusted, and laboratory tests, such as will be outlined later in this article, should be carried out.

C. Syphilis of the Conjunctiva: In syphilis of the conjunctiva, the induration is always so well marked that one would not confound the soft vegetations of Parinaud's conjunctivitis or the nodular swellings of tularemia with the indurated surface in syphilis. The erosive surface of the chancre is usually covered over by a pseudomembranous exudate.

2. *Severe Conjunctivitis Caused by a Small Gram-Negative Bacillus.* —This condition so closely resembles tularense conjunctivitis that it might be identical.

A. Necrotic Infectious Conjunctivitis (Pascheff): In 1914, Professor Pascheff of Sofia described three cases of a peculiar conjunctivitis, which he studied carefully. The disease began with malaise, loss of appetite and increase in temperature. Only one eye was affected. The preauricular and submaxillary lymph glands were enlarged on the affected side. Locally, the condition began with itching and redness of the lids. The borders of the lids became thickened. Moderate photophobia and lacrimation were present. The tarsal conjunctiva and conjunctiva of the fornix were somewhat thickened by infiltration, but were smooth. Minute points and spots, which varied in size, were seen in the conjunctiva, especially in that of the tarsus and fornix. The spots had ill defined edges, entirely superficial, and when their surface was rubbed, some necrotic tissue was scraped away and a shallow superficial ulcer was left, which healed without a scar. The disease has three stages: (1) formation of conjunctival necrotic areas; (2) stage of ulceration; (3) stage of repair. The conjunctival process covers between two and three weeks. The involvement of the lymph glands lasts longer than the conjunctivitis, and the skin covering them is red and painful to the touch.

"Material injected intraperitoneally into a guinea-pig resulted in the death of the animal in 7-8 days. The spleen showed small white areas" (abstract from Ophth. Year Book, vol. 16, 1920, p. 68).

The organism named *Micrococcus polymorphous necroticans* is gram-negative, grows well on ordinary mediums and differs in other cultural characteristics from the tularense bacillus.

In my opinion, however, its claim as a separate disease entity rests mainly on the fact that pure cultures are said to cause the disease on inoculation into guinea-pigs. Professor Pascheff, however, did not

send specimens of blood from his patients to Francis as the latter requested, so that agglutination tests with *B. tularense* might be carried out.

Except for Pascheff's cases, no other case reports on this disease have reached my attention. H. H. Stark of Texas reported four cases of conjunctivitis, which he arbitrarily called Pascheff's disease. Except for smears and cultures which were negative, no laboratory studies were made, and his paper is consequently of no importance. As far as the clinical descriptions go, his cases could have been, and probably were, cases of tularemia.

B. Conjunctivitis Pseudotubercle Rodentium: In 1919, Bayer and von Harrenschwand found in two cases of conjunctivitis numerous small nodules which either progressed to ulceration or were absorbed without scars. The preauricular and cervical glands of the same side were affected. The cause was a variety of *Bacillus pseudotuberculosis rodentium,* an organism which closely resembles *Bacillus tularense.*

3. *Sporotrichosis.*—In 1909, Morax reported the first case of sporotrichosis of the conjunctiva. Gifford reported the next case and Bedell the next; finally, Wilder and McCullough, in a classic paper published in 1914, described a case which showed small yellow ulcers on the conjunctiva and lymph adenopathy.

The description in Fuch's "Textbook of Ophthalmology" sums up the knowledge concerning this disease, as follows:

> This rare disease is caused by various species of sporotrichon and produces small, light yellow, soft nodules in the conjunctiva with points of ulceration and with purulent discharges. There is swelling of the neighboring lymph glands. Nodules also occur in the lid margin. The canaliculi may contain concretions enclosing the sporotrichon.

A culture on any of the usual mediums is so characteristic that it cannot be mistaken for anything else. It develops in from three to ten days.

4. *Agricultural Conjunctivitis.* — Patten and Gifford, in 1921, described a severe monocular conjunctivitis with involvement of the regional lymph glands, the chief characteristics of which are: (1) pronounced swelling and redness of the lids (2) involvement of the regional lymph nodes, (3) the presence of more or less extensive skin lesions and (4) a dense and decidedly adherent false membrane. The temperature may be from 99.5 to 101 F. at the start, dropping to normal in a few days.

This disease should not be confused with tularemia, since no cases of the latter showed a false membrane at any time.

5. *Other Conjunctival Diseases.*—Other conjunctival diseases which might simulate tularemia are streptothrix and acute trachoma.

LABORATORY STUDIES TO BE CARRIED OUT IN A CASE OF PARINAUD'S SYNDROME

In 1924, Pascheff suggested the substitution of the term Parinaud's syndrome in a place of Parinaud's conjunctivitis as signifying a unilateral conjunctivitis with regional lymphadenitis. This term has since been adopted by various authors and should be more generally utilized.

All cases, then, presenting a unilateral conjunctivitis with lymphadenopathy should be carefully studied, as follows, in order to discover the etiologic factor:

Smears and Cultures.—The cultures may show *Sporothrix*. If egg-yolk medium is used, inoculation done under partial tension and anaerobic conditions carried out, one might succeed in growing *Leptothrix* as Wherry and Ray have done (*J. Infect. Dis.* **22**:554, 1918).

Conjunctival Scrapings Injected Into a Guinea-Pig.—When conjunctival scrapings are injected into a guinea-pig tularemia may occur in six or seven days.

Excision of Conjuntival Lesion.—When the conjunctival lesion is excised, half of the material should be used for studies of the microscopic changes. (*a*) This is of importance, since so far there has been no description of the histology of an ocular lesion in tularemia. (*b*) A section should be stained by Verhoeff's method to demonstrate *Leptothrix*. (*c*) A section might show typical foci of tuberculosis.

The other half should be emulsified and injected intraperitoneally into a guinea-pig. This is to demonstrate tularemia, tuberculosis or Pascheff's organism. It is possible that the new potato medium discovered by Corper and Uyei can be utilized to grow the tubercle bacilli.

Blood from the Patient.—Enough blood should be taken to perform a Wassermann test and to be sent to Dr. Edward Francis, the Hygienic Laboratory, 25 E Street, Washington, D. C., for agglutination tests for tularemia.

Differential Blood Count for Eosinophilia.—If the foregoing studies are carefully carried out, there will be few cases of Parinaud's syndrome, the etiologic factor of which remains an unknown quantity.

TREATMENT OF OCULAR TULAREMIA

There is no specific treatment. A vaccine has been used in two cases (those of Lamb and Vail, Jr.), with a marked febrile reaction resulting. Wherry suggested that this might be of value in diagnosis, acting at least much like the Mallein test in glanders. The therapeutic value of vaccines, however, is doubtful. In spite of frequent instillation of mercurochrome-220 soluble for twenty-four hours in one case (that of Vail, Jr.), Wherry succeeded in killing a guinea-pig with the bacillus obtained from a conjunctival scraping.

Protargin mild solution, strong silver protein, neo-silvol, boric acid solution and the other usual collyria have been used without any specific action.

Perhaps the best local treatment, in view of the limited knowledge in this respect, is continuous hot applications of magnesium sulphate, physiologic solution of sodium chloride and frequent lavage of the con-

junctival sac with a mild antiseptic solution, such as boric acid, sodium biborate or even saline solution.

The general treatment should be supportive and the usual measures in a febrile disease carried out.

If the glands suppurate, they should be incised.

BIBLIOGRAPHY

Tularemia

Wherry, W. B.: Plague Among the Ground Squirrels of California, J. Infect. Dis. **5**:485, 1908.

McCoy: Plague-Like Disease in Rodents, Bull. 43, U. S. P. H. S., April, 1911, p. 53.

McCoy and Chapin: B. Tularense, the Cause of the Plague-Like Disease of Rodents, Bull. 53, U. S. P. H. S., 1912, p. 21.

Vail, D. T., Sr.: Bacillus Tularense (Squirrel Plague) Infection of the Eye, Ophth. Rec. **23**:487, 1914. The first textbook description of the disease is found in the American Encyclopedia of Ophthalmology, New York, William Wood & Company, 1917, vol. 5, p. 3157.

Wherry, W. B., and Lamb, B. H.: Infection of Man with Bacterium Tularense, J. Infect. Dis. **15**:331, 1914.

Sattler: Bacillus-Tularense Conjunctivitis, Arch. Ophth. **44**:265, 1915.

Wherry and Lamb: Discovery of B. Tularense in Wild Rabbits and the Danger of Its Transfer to Man, J. A. M. A. **63**:2041 (Dec. 5) 1914.

Lamb, F. W.: Conjunctivitis Tularensis with Report of a Case, Ophth. Rec. **26**: 221, 1917.

Pfunder: Primary Tularemia of the Eye, J. A. M. A. **85**:1061 (Oct. 3) 1925.

Martin: Tularemia Infection of Conjunctiva, Southwestern Med. **9**:232 (June) 1925.

Vail, D. T., Jr.: A Case of B. Tularense (Squirrel Plague) Conjunctivitis, Arch. Ophth. **55**:235, 1926.

Martin, Ancil: Tularemia, Southwestern Med. **10**:249 (June) 1926.

Freese; Lake; and Francis: Four Cases of Tularemia (Three Fatal) with Conjunctivitis, U. S. Public Health Rep., Feb. 26, 1926.

Gillette, W. G.: Tularemia, J. Kansas M. Soc. **25**:77, 1927.

Morrison, W. R.: Tularemia and Parinaud's Conjunctivitis, correspondence, J. A. M. A. **87**:607 (Aug. 21) 1926.

Jackson, Z. H.: Report of a Case of Conjunctivitis Tularensis, J. M. A. Georgia **16**:44, 1927.

Flick, John: Tularemia, Ann. Surg. **83**:737, 1926.

Magath and Yater: Tularemia, Clin. N. Amer. **10**:745 (Nov.) 1926.

Barry, A. C.: Two cases of Tularemia, Nebraska M. J. **12**:191, 1927.

Junkin, H. D.: Two Unusual Cases of Tularemia, Nebraska M. J. **12**:191, 1927.

Clark, C. P.: A Typical Conjunctivitis Tularensis, Northwest Med. **26**:415, 1927.

Fuller, T. E.: Parinaud's Conjunctivitis, Am. J. Ophth. **1**:499, 1918.

Francis, Edward: Deer-Fly Fever; A Disease of Man of Hitherto Unknown Etiology, U. S. Pub. Health Rep., 1919, vol. 34, p. 2061.

Francis, Edward; and Moore, Dunlop: Identity of O'Hara's Disease and Tularemia, J. A. M. A. **86**:1329 (May 1) 1926.

Pearse, R. A.: Insect Bites, Northwest Med., March, 1911.

Golov, Kniazevsky; Berkinkov, and Tiflov: Pestiform Affections (Tularemia?) in the Region of the Basin of the Ural in Spring, 1928, Rev. de microbiol. d'epidemoil, et de parasitol. **7**:301, 1928.

Francis: Summary of Present Knowledge of Tularemia, Medicine **7**:411, 1928.
Simpson, W.: Tularemia; A Clinical and Pathological Study of Forty-Eight Nonfatal Cases and One Rapidly Fatal Case, with Autopsy, Occurring in Dayton, Ohio, Ann. Int. Med. **1**:1007, 1928.
Personal communication to the author.
Tularemia, New York, Paul Hoeber, 1929.
Parinaud's Conjunctivitis
Morax: French Encycl. Ophth., 1910, vol. 5, p. 774.
Gifford, H.: Five Cases of Parinaud's Conjunctivitis (case 1 might have been tularemia), Ann. J. Ophth., July, 1898, p. 193.
Morax, V.: Parinaud's Conjunctivitis, Brit. J. Ophth. **11**:133, 1918.
Purtscher, A.: Relation of Conjunctivitis Tuberculosis to Parinaud's Conjunctivitis, Ztschr. f. Augenh. **46**:187, 1921.
Weaver and Gillette, W. G.: Parinaud's Conjunctivitis with Eosinophilia, Ann. J. Ophth. **6**:36, 1923.
Gifford, S. R.: Eosinophilia and Etiology of Parinaud's Conjunctivitis, Ann. J. Ophth. **8**:450, 1925.
Spritze: Parinaud's Conjunctivitis (case 1 may have been Tularemia), Am. J. Ophth. **34**:364, 1917.
Leptothrix Conjuncivitis (Verhoeff)
Verhoeff, F. W.: Parinaud's Conjunctivitis, Arch. Ophth. **42**:347, 1913.
Observations on Parinaud's Conjunctivitis (Leptothricosis Conjunctivae), Am. J. Ophth. **1**:705, 1918.
Gifford, S. R.: Parinaud's Conjunctivitis (Leptothricosis Conjunctivae), Am. J. Ophth. **10**:484, 1927.
Wherry and Ray: J. Infect. Dis. **22**:554, 1918.
Tuberculosis of the Conjunctiva
Tomassene, R. A.: Parinaud's Conjunctivitis, Am. J. Ophth. **11**:721, 1928.
Bartos and Motto: Tuberculosis of the Conjunctiva, Am. J. Ophth. **11**:533, 1928.
Thompson, J. J.: Primary Tuberculosis of the Conjunctivae, Ann. Ophth. **20**:76, 1906.
Corper and Uyei: New Method for Cultivating Tubercle Bacilli, J. Lab. & Clin. Med. **14**:393, 1929.
Necrotic Infectious Conjunctivitis (Pascheff)
Pascheff, C.: Inflammation of Conjunctiva (Necrotic Infectious), Klin. Monatsbl. f. Augenh. **57**:517, 1919.
Necrotic Infectious Conjunctivitis, Arch. d'opht. **38**:23, 1921.
Abstract from Ophth. Year Book **16**:68, 920.
Differential Diagnosis Between Parinaud's Conjunctivitis and Conjunctivitis Necroticans Infectiosa, Brit. J. Ophth. **8**:25, 1924.
Differential Diagnosis Between Conjunctivitis Necroticans Infectiosa and Conjunctivitis Tularensis, Am. J. Ophth. **10**:737, 1927.
Stark, H. H.: Conjunctivitis Infectiosa Necroticans, Tr. Sect. Ophth., A. M. A., 1924, p. 56.
Conjunctivitis Pseudotubercle Rodentium
Bayer and von Herreschwand: Pseudotubercle Bacilli in Production of Conjunctivitis, Arch. f. Ophth. **98**:342, 1919.
Rosenstein: Parinaud's Conjunctivitis, Klin. Monatsbl. f. Augenh. **69**:71, 1922.
Sporotrichosis
Gifford, H.: Sporotrichosis of the Eyeball and Eyelids, Ophth. Rec. **19**:573, 1910.
Morax, V.: Ann. d'ocul., May, 1909, p. 329.

Bedell, A. T.: Chronic Sporotrichosis of Eye, Ann. Ophth. **23**:605, 1914.

Wilder, William H., and McCullough, C. P.: Sporotrichosis of the Eye, J. A. M. A. **62**:1156 (April 11) 1914.

Wilder: Ocular Sporotrichosis, Arch. Ophth. **43**:161, 1914.

Fuchs: Textbook of Ophthalmology, Philadelphia, J. B. Lippincott Company, 1923, p. 475.

Agricultural Conjunctivitis

Patten and Gifford: Agricultural Conjunctivitis, Tr. Sect. Ophth., A. M. A., 1921, p. 226.

Discussion from Stark, H. H.: Tr. Sect. Ophth. A. M. A., 1924, p. 60.

GLUTATHIONE IN THE CRYSTALLINE LENS *

I. S. TASSMAN, M.D.
AND
W. G. KARR, PH.D.
PHILADELPHIA

The soluble portion of the lens protein has been the subject of considerable interest and study since the time of Moerner,[1] who showed that it was composed almost entirely of the two crystallines which represented in great part the sulphur content. The nitroprusside reaction, which was described by Arnold [2] in 1911, showed that the normal lens when treated with a 5 per cent solution of sodium nitroprusside and a drop of ammonia will turn a decided red, resembling the color of permanganate. In studying senile cataract, Reiss [3] and Jess [4] found that whereas this reaction was positive with the normal lens, it was negative in those parts of the lens that had become cataractous. In mature senile cataract, the red color which was produced ordinarily was entirely absent. Since the positive reaction was said to be caused by the amino-acid cysteine, it was concluded from the result of the reaction that this substance was present in the normal lens and absent as such in the cataract lens. The results of this qualitative test have been confirmed by us many times; recently also, Cohen and Killian [5] published a report of sixty-four cataract lenses so tested, in which they obtained similar results.

Heffter,[6] in studying cysteine and its possible importance in the tissues, pointed out that the substance constantly undergoes an oxidation-reduction whereby it changes from the reduced form cysteine to the oxidized form cystine and then back again. He described this oxida-

* Submitted for publication, June 11, 1929.

* From the departments of Ophthalmology and Bio-Chemistry, Graduate School of Medicine, University of Pennsylvania.

1. Moerner, T.: Untersuchung der Proteinsubstanzen in den lichtbrechenden Medien des Auges, Ztschr. f. physiol. Chem., 1893, vol. 18.

2. Arnold: Eine Farbenreaktion von Eiweisskörpern mit Nitroprussidinatrium: Ueber den Cystein gehalt der tiereschen Organe, Ztschr. f. physiol. Chem., 1911, vol. 70.

3. Reiss, W.: Ueber die Cysteinreaktion der normal und pathologisch veränderten Linse, Arch. f. Ophth. **80**:588, 1911.

4. Jess, A.: Zur Chemie der Cataracta senilis, Arch. f. Augenh. **71**:3, 1912.

5. Cohen and Killian: Sulphur Partition of Ocular Humors and Presence of Glutathione in Lenses of the Eye, Proc. Soc. Exper. Biol. & Med. **25**:677, 1928.

6. Heffter: Die Reduzierenden Bestandteile der Zelle, Medz. Naturw. Arch., vol. 1, Referiert in Jahresb. ü. d. Fortschr. d. Therchem. **37**:565, 1907.

tion-reduction as a reversible process, and attributed it to the action of the labile hydrogen of the SH radical present in its molecule. The nitroprusside reaction, which is positive with cysteine, the reduced form, is negative with cystine, the oxidized form. Although cysteine had not been demonstrated in the tissues in its free state, Heffter spoke of its reversible oxidation-reduction activity as an important factor in cell metabolism in the tissues.

In 1921, however, Hopkins[7] in the course of an investigation discovered a dipeptide which he named glutathione, and which he demonstrated as a combination of cysteine and glutamic acid. He first produced this substance from yeast, and later showed that it was present in the liver and other organs. He showed that it also exhibited the same reversible oxidation-reduction property formerly attributed to cysteine, and that in its reduced form it displayed a positive nitroprusside reaction, whereas this reaction was negative with the substance in its oxidized form. Hopkins felt that glutathione exercises real functions in the chemical dynamics of the cell, and he described its oxidation-reduction under the influence of factors shown to be present in the tissues. He explained that being autoxidizable, it readily acts under varying conditions both as a hydrogen acceptor and a hydrogen donator, owing to changes in the sulphur group of its cysteine constituent. As a result, it changes from the sulphydryl to disulphide form and vice versa.

$$-SH\ \ HS- \rightleftarrows -S-S- + H_2$$

TABLE 1.—*Hopkins' Results of the Estimation of Glutathione*

Tissue	Per Cent	Range, per Cent
Yeast (fresh)	0.18	0.15 to 0.22
Liver (rat)	0.18	0.16 to 0.21
(rabbit)	0.24	0.22 to 0.35
Skeletal muscle (rat)	0.034	.....
(rabbit)	0.04 to 0.045	.....

Hopkins' results of the estimation of glutathione appear in table 1.

From these results it can be seen that he obtained the largest percentage of glutathione in the liver.

Now if, as Heffter and also Hopkins pointed out, the presence of cysteine or glutathione is essential to efficiently functioning cells, and since we know that the nitroprusside reaction which is produced by it is positive in the normal lens and negative in the cataract lens, it would be of interest to the ophthalmologist to know of the quantitative presence of this substance in both the normal and the cataract lens. With this in mind, we were led to attempt such a determination.

7. Hopkins: Biochem. J., 1921, vol. 16; 1923, vol. 17; 1925, vol. 19.

M. Goldschmidt,[8] in analyzing the two lenses in animals of various ages, estimated that the cysteine decreases in older animals. In this he employed an older method and made no mention of the weights of the lenses but appears to have been guided only by the ages of the animals. Recently Michail and Vancea [9] reported an analysis, according to the method of Tunnecliffe, of reduced glutathione in the lens of oxen, rabbits and dogs, in which they obtained a constant result of 356 mg. In the other parts of the eye they found the percentage much lower. It will be noted that their result in the lens is much higher than that found by Hopkins in the liver. In this respect our own results, though generally lower, compare favorably.

EXPERIMENTAL WORK

We attempted, first, to establish the percentage of glutathione in the freshly obtained normal lens of the pig; then in other freshly obtained normal lenses we estimated the percentage of total cystine. With the results obtained, an equilibrium

TABLE 2.—*Percentage of Dry Matter in Normal Pig Lens*

Experiment	Fresh Lens, Gm.	Dried Lens, Gm.	Dry Matter, per Cent
1	7.03	2.20	31.3
2	10.52	3.30	31.4

ratio between cysteine and cystine could be determined in the normal lens of the pig. Samples of human cataract lens immediately after extraction were then examined, first for glutathione and then for the total cystine, as in the normal lens of the pig. The results obtained appeared conclusive, since no glutathione was found in the cataract lenses. The percentage of total cystine here obtained was lower than that of the normal lens of the pig, but in cataract lens it represented all oxidized cystine.

Normal Lens of the Pig.—First, the percentage of dry matter was determined as follows: A quantity of normal freshly extracted lens was weighed in a glass dish, placed in a vacuum desiccator and dried to constant weight. An average of 31.35 per cent of dry matter in normal pig lens was thereby obtained.

To determine the glutathione, eyes were removed from pigs of uniform age and weight, immediately after death, and were brought to the laboratory at once. The lenses were removed and were immediately weighed. The glutathione content was estimated by the Perlzwig and Delrue [10] modification of the Tunnecliffe method.[11] From this series of seven experiments, an average percentage of 0.296 of glutathione was obtained in the normal lens of the pig.

8. Goldschmidt, M.: Beitrag zur Physiologie und Pathologie der Krystallinse, Arch. f. Ophth., 1917, vol. 93.

9. Michail, D., and Vancea, P.: Sur la teneur en glutathion reduit des tissus oculaires normaux, Compt. rend. Soc. de biol. **99**:891, 1928.

10. Perlzwig, W. A., and Delrue, Georges: The Use of the Starch-Iodine End Point in Tunnecliffe's Method for the Determination of Glutathione in Tissues, Biochem. J. **21**:1416, 1927.

11. Tunnecliffe: The Occurrence and Quantitative Estimation of Glutathione in Tissues, Biochem. J. **19**:194, 1925.

Next a sample of fresh lens which had been vacuum dried to constant weight over a period of from three to four weeks was examined in the same way. The process of desiccation reduced the content appreciably. The weight of the dried lens was 0.5 Gm.; 2.8 cc. of hundredth normal iodine was used, and the percentage of cysteine was 0.7. Calculated on the basis of the original wet lens, the cysteine amounted to 0.222 per cent.

A sample of wet lens was next obtained and extracted with 5 per cent trichloracetic acid. The extract was allowed to stand at room temperature for twenty-four hours before being titrated with the iodine. It was found that the glutathione content was markedly reduced. The lens mass weighed 2.66 Gm.; the hundredth normal iodine used was 3.2 cc., and the percentage of cysteine was 0.106.

The cystine in the normal lens of the pig, obtained as described, was estimated by the method of Folin and Looney.[12] These results include cystine in both the oxidized and the reduced forms. Five determinations were made, and the following data were obtained for the percentage of total cystine in the wet lens: 0.894, 0.970, 1.02, 1.04 and 1.07. From these results, the average total cystine in normal

TABLE 3.—*Glutathione Content of the Normal Lens of the Pig*

Experiment	Lens Mass, Gm.	N/100 Iodine, Cc.	Cysteine, per Cent
1	5.37	12.1	0.282
2	3.27	6.8	0.261
3	3.41	8.2	0.301
4	2.83	6.55	0.289
5	3.28	9.55	0.304
6	3.135	7.0	0.279
7	3.145	7.0	0.300

pig lens was estimated as about 1 per cent. The average equilibrium ratio between cysteine and cystine obtained thereby is $\frac{0.296}{0.704}$, or 0.420. (The cystine present as such in original lens is obtained by subtracting the cysteine figure from the average total cystine.)

Human Cataract Lens.—Mature human cataract lenses were weighed immediately after being extracted and were placed in alcohol. After a sufficient quantity had been obtained, they were removed to a tared dish, the alcohol was evaporated and the residue was vacuum dried. The weight of the lens mass was 2.115 Gm., that of the dried lens, 0.75 Gm. The percentage of dry matter was 35.5, which was greater than that in the normal lens of the pig.

Glutathione was estimated in the human cataract lens as in the normal lens of the pig. The lenses were extracted with 5 per cent trichloracetic acid and titrated with hundredth normal iodine within one hour after removal from the eyes. Two experiments yielded the same result. In the first experiment there was so little material used (0.31 Gm.) that an exact estimation could not be made, but it was determined that the lenses contained no glutathione. In the second experiment, with a larger amount of material (0.83 Gm.), it was found that no titrable amount of iodine was used, and that therefore, as nearly as could be determined, no glutathione was present.

12. Folin, Otto; and Looney, J. M.: Colorimetric Methods for the Separate Determination of Tyrosine, Tryptophane and Cystine in Proteins, J. Biol. Chem. **51**:421, 1922.

The total cystine in 0.5 Gm. of desiccated human cataract lens was estimated by the method of Folin and Looney. It was found to contain 2.25 per cent of cystine. Since the dry matter had been calculated at 35.5 per cent of the original wet lens, the result of total cystine estimated was 0.8 per cent in the human cataract lens. This was lower than the total cystine content of the normal lens of the pig. The total here, however, represents all oxidized cystine, since none of the reduced form was found in the cataract lens.

COMMENT

From these results it can be seen that glutathione is present in the normal lens of the pig in definite amount (0.296 per cent), and that an equilibrium ratio was established between cysteine and cystine ($\frac{0.296}{0.704}$ or 0.420); in cataract lens it was determined that glutathione was entirely absent.

If it is assumed that in the crystalline lens as in other tissues there normally exists a constant oxidation-reduction potential or balance, an interesting possiblity is introduced whereby in cataract formation something might occur which would cause a disturbance of the normal equilibrium and therefore interfere with the reversible oxidation-reduction process. Various influences on the oxidation and reduction of cysteine and glutathione have been studied from time to time. Jess [13] showed that light has no effect on the normal lens after exposure to the rays of the quartz lamp. He found after numerous tests that the nitroprusside reaction was positive after irradiation as it was before.

Abderhalden and Wertheim [14] obtained the same results in their investigations. In addition they also studied the effect of other influences on the oxidation-reduction, employing the nitroprusside reaction as a guide. They showed that increased temperature hastens oxidation; in acid reaction it was retarded, whereas in alkaline reaction it took place rapidly. Of the metals, iron was found to hasten the process, as did copper, mercury and arsenic, although not so strongly. Potassium cyanide, lead, nickel, cobalt and cadmium were found to retard oxidation.

According to Thompson and Voegtlin,[15] glutathione is specifically concerned in the chemical defense of the body against the action of certain poisons, such as arsenic, copper, gold, cyanide and methylene blue (methylthionine chloride, U. S. P.). They believed that the toxic action of these substances is due to a primary disturbance of the cellular oxidation-reduction processes resulting from a chemical interaction of

13. Jess, A., and Kochella, S.: Ueber den Einfluss des Ultravioletten Lichtes auf die Cysteinreaktion der Linse, Arch. f. Ophth., 1923, vol. 8.

14. Abderhalden and Wertheim: Studien über Autoxydation, Arch. f. d. ges. Physiol. **197**:131, 1922.

15. Thompson, J. W., and Voegtlin, Carl: Glutathione Content of Normal Animals, J. Biol. Chem. **70**:793, 1926; Glutathione Content of Tumor Animals, ibid. **70**:801, 1926.

the poison with the glutathione of the cells. In their series of experiments, they determined an average of about 0.183 per cent of glutathione in the liver of the rat. In a study of mammalian tumor growths, they found a percentage of glutathione comparable to that found in the liver.

A great deal remains to be explained concerning the chemical alterations of the crystalline lens in vivo. Changes in the surrounding media, an increased permeability of the capillaries and changes in the permeability of the lens capsule which would permit deleterious substances to come in contact with the lens, thereby causing its chemical alteration, are some of the important factors considered in the investigation of cataract formation. That the normal state or activity of glutathione in the lens could be disturbed by such changes is also a possibility.

HEREDITARY NYSTAGMUS

REPORT OF A CASE *

WILLIS S. KNIGHTON, M.D.
NEW YORK

Nystagmus is a series of more or less rapid vibrations that take place when the eye is in or near the primary position. In direction, the oscillations are generally horizontal, but they may be vertical, rotary or mixed. The frequency varies from 60 to 200 separate oscillations per minute, and the extent of the excursions from 1 to 10 mm. True nystagmus is almost always binocular, and the movements are conjugate, i. e., equal, simultaneous and parallel in the two eyes. This means that the two eyes act alike; it does not imply that the two components of the oscillations are equal, for, as is well known, there are two distinct types of oscillation, the springing or resilient and the pendulum.

The resilient type of nystagmus has a slow component in one direction which is immediately followed by a quick return. The slow component is vestibular and is characteristic of disturbances of innervation in the labyrinth. The quick return is cerebral. Resilient nystagmus occurs in labyrinthine suppuration, after the caloric and Bárány tests in normal patients, in cerebellar abscess and tumor, in tumors of the cerebellopontile angle, in Friedreich's ataxia, multiple sclerosis, encephalitis, syringomyelia, Little's disease and idiocy. It may also follow the consumption of large amounts of alcohol and certain poisons.

Pendulum, or undulating nystagmus, where both components are equal in time and extent, is the distinguishing mark of cases characterized by a faulty retinal image. It depends for its existence on the use of the eyes, and is thought by Dunphy to make its appearance about the time when coordinate movements of the eyes are developing. The genesis of the nystagmus is explained by Duane as a reflex movement of the eyes in an attempt to discover the most acute part of the retina for fixation. Ordinarily, movement ceases as soon as macular fixation is obtained, but in these cases of visual nystagmus in which bilateral amblyopia is always present, macular fixation is not sufficiently acute, and the eye swings on until increasingly imperfect peripheral vision starts it in the opposite direction. Duane added that if fixation has been acquired before amblyopia begins, nystagmus fails to develop.

The conditions causing amblyopia in these cases are opacities of the cornea (especially from ophthalmia neonatorum) and media, con-

* Submitted for publication, June 14, 1929.

* Presented before the Section of Ophthalmology, New York Academy of Medicine, April 15, 1929.

genital cataract, hemorrhage, disease, abnormalities of the retina and choroid, total congenital color blindness and albinism.

In the consideration of nystagmus in general, Nettleship expressed the opinion that idiosyncrasy, the personal equation, plays a large part, and that this liability may be heritable.

Nystagmus of the central nervous system, spasmus nutans, nystagmus following ocular disease, miners' nystagmus (an occupational form occurring later in life), etc., are similar in two respects: 1. The oscillation comes on a considerable time after birth. 2. It is not associated with any defect in visual acuity unless that defect is due to obvious congenital or infantile disease of the eye.

Hereditary nystagmus, on the other hand, appears shortly after birth and is usually associated with defective vision but with no signs of disease, past or present. Dunphy found hereditary nystagmus neither visual nor vestibular in origin, placing it in a separate group, and Nettleship, who made a special study of these cases, seemed of the same opinion although he felt that there are not sufficient data to warrant an arbitrary classification. He also questioned whether the amblyopia brings on the nystagmus or whether the nystagmus causes or heightens the amblyopia.

Nettleship assumed that these patients have an inherited disposition to nystagmus which may remain latent until excited by some other defect (often itself inherited) that diminishes the value of steady fixation and gives a free rein to nystagmus. There is no evidence of nystagmus existing at birth or before the use of the eyes, else this explanation would not hold. The exciting abnormality usually takes the form of defective vision due to a deficiency of ocular pigment or a considerable ametropia, or both. Hemmes found the astigmatism fairly high in about two thirds of the cases.

The deficiency in ocular pigment is never great, taking the form of blue or gray irides, sometimes lightly pigmented choroids and hair, but never going beyond incomplete albinism. As regards incomplete albinism, it is questionable whether it is ever sufficiently marked to cause amblyopia and nystagmus. Microscopic examination is urged in these cases to determine whether the retinal epithelium is adequately pigmented.

Yawger felt that many nervous diseases and disorders are etiologic factors. Frankenberg could find no pathologic process in one of his cases which came to autopsy, and concluded with Lenoble and Aubineau that hereditary nystagmus is a degenerative symptom.

Hereditary nystagmus may descend in either of two ways. In the first, or ambisexual group, it descends through either parent, but more often through the father, and affects both sexes; in the second,

or male-limited group, it descends through unaffected females and is limited to the males. The latter mode of descent is relatively rare.

Burton and others reported cases in which vision and refraction were normal and the fundi appeared well pigmented. These cases are rare and occur chiefly in the ambisexual group, as do also the equally rare cases in which the patients have dark complexions and well pigmented irides. Cockayne reported three cases in the same family in which the males alone were affected. Their cases agree with other published cases in that no head movements were present, but they differ in that the vision was good and there was well marked pigmentation of the choroids and irides. This is unusual in the male-limited group.

The head movements which are occasionally found in the ambisexual group are not to be confused with spasmus nutans, the head-shaking of infants. The latter is generally due to poor illumination and does not appear until several months after birth. It is a benign disease in which recovery invariably occurs, often as soon as the illumination near the crib is improved, whereas the head movements associated with hereditary nystagmus are much more persistent.

Other congenital defects may exist with hereditary nystagmus, but their association is inconstant. Lenoble and Aubineau reported several cases associated with trophic or nervous disturbances. This type was frequent among the rather degenerative population in Brittany; hence their assumption that race is an etiologic factor.

Hemmes found the irritability of the horizontal semicircular canals diminished or abolished in all of the patients he examined.

Consanguinity apparently plays a small rôle; there is no history of it in the vast majority of cases, although Coburn found definite evidence of it in one of his, and Cockayne seemed inclined to assume its presence in others.

The report of my case follows.

REPORT OF A CASE

W. A., a Jew, aged 37, had had nystagmus and poor vision since infancy. The poor vision had remained the same as far as he could remember, and at the time of examination was as good as it ever had been. He also gave a history of hemophilia and complained of being unable to see at night. His general condition was excellent and had always been so.

Several other members of the family were similarly affected with nystagmus and poor vision. Some of them were supposed to be hemophiliac, and one of them, the patient's son, had head-shaking in addition. Unfortunately, I was unable to examine any other members of the family. There was no history of consanguineous marriage as far back as the pedigree went, nor was there any record of other congenital or hereditary defects.

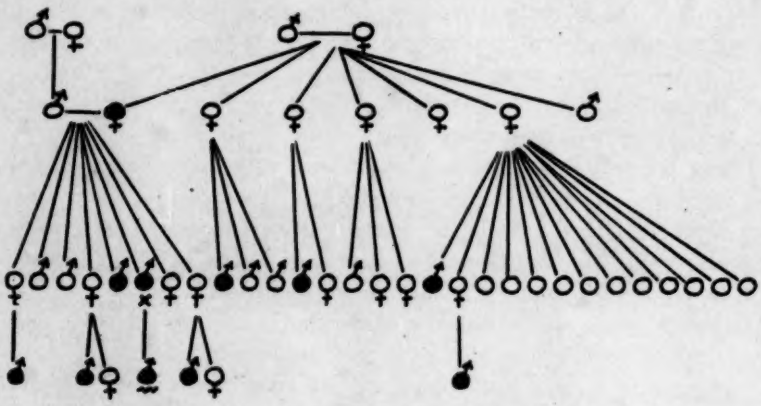
The patient's vision was 20/100 in the right eye and 20/200 in the left. The error of refraction was noticeably small: right eye, $+.25 \bigcirc +.50 \times 135°$, and

left eye, + .75 ⊂ + 1.25 × 60°, but correction did not improve the vision. In spite of this, the patient was able to carry on his business, which involved a considerable amount of desk work, play cards and enjoy the theater, an observation which was hardly consistent with his complaint of poor vision at night. With telescopic lenses containing the foregoing corrections, the vision could be brought up to 20/40 in the right eye and 20/70 in the left, but the patient preferred not to wear these glasses because of their appearance.

There was a horizontal pendulum nystagmus, equal in both eyes, with a frequency of about 2 to 3 per second, which was increased slightly on looking extremely to either side. Vestibular irritation was present and equal on both sides but was slightly reduced. This was in accord with most observations.

The left eye diverged 15 degrees on the perimeter and swung out to 30 degrees under cover. The image in the left eye was usually suppressed. The anterior part of each eye was normal.

The irides were grayish and of the same pigmentation. The lenses were clear with no sign of posterior cortical involvement. There were fine dustlike opacities



Hereditary nystagmus in the ambisexual group.

in the vitreous of the right eye but none in the left. The fundus appeared well pigmented, and there was no obvious pathologic process in the macular region. Both optic disks were pale, and the retinal blood vessels were reduced in caliber, suggesting retinitis pigmentosa sine pigmento. Although the history was not typical of that disease, the fields for form were concentrically contracted about 15 degrees and the color fields proportionately more, presenting the "depression" field which Traquair said may occur in congenital hereditary night blindness. This may be the other defect of which Nettleship spoke, which set off the latent tendency to nystagmus. The blind spots were not enlarged. No scotomas were found, although the eye was not fixed during the examination, and it is possible that they were masked by the oscillations. After exposure to a strong light, the patient's dark adaptation was normal as compared with my own.

The Wassermann reaction was negative and had been at every other test.

Results of the examination of the ear, nose and throat had always proved negative, except for the slightly reduced irritability of vestibular stimulation.

The bleeding time and coagulation time were normal, being two minutes and a half, and five minutes, respectively. In spite of this, the patient insisted that he was a bleeder.

The pedigree is interesting. In the chart the patient is shown in the third generation, no. 6 from the left over the mark *x*. The patient's mother was the only female who was similarly affected. In every other case the disease was transmitted through unaffected females to the males only, except that the patient himself transmitted it to his son. Were it not for this single line of descent, this would be an excellent illustration of the male-limited group. As it stands, there is no question that it is other than ambisexual, but it would be interesting to be able to follow the pedigree through for several more generations to see whether it will eventually fall into the second mode of descent.

No. 4 in the fourth generation is the only patient with a definite history of head-shaking. He is now about 7 years old, and the head movements have lessened considerably.

After the second generation, about two thirds of the males are affected. They are all in good general health, of about the same complexion as my patient, and all have greatly reduced vision which cannot be improved.

There is no history of nystagmus or reduced vision on the paternal side of my patient's pedigree; all of the known instances occur on the maternal side, although the maternal grandparents are themselves unaffected.

SUMMARY

This case is presented for the following reasons:

1. The symptoms and pedigree are typical of hereditary nystagmus.
2. The refractive error is unusually small.
3. There is a possible accompaniment of retinitis pigmentosa sine pigmento.
4. The pedigree is obviously ambisexual, but with the exception of a single line of descent, would serve to illustrate male-limited heredity.

BIBLIOGRAPHY

Burton: Hereditary Congenital Nystagmus, Lancet **2**:1497, 1895.

Coburn: Congenital Nystagmus, Ophthalmology Year Book, 1908, vol. 5, p. 109.

Cockayne, E. A.: Demonstration of Cases of Nystagmus, Proc. Roy. Soc. Med., Sec. Neurol. Ophth. & Otol. **7**:6 (Feb..26) 1914.

Duane, A., in Fuchs: Textbook of Ophthalmology, ed. 8, Philadelphia, J. B. Lippincott Company, 1924.

Dunphy, E. B.: Nystagmus, Boston M. & S. J. **194**:539, 1926.

Fisher, T.: Congenital Nystagmus in Father and Child, Brit. M. J., 1902.

Frankenburg, R.: Hereditary Nystagmus, Inaug. Diss., Göttingen, 1909.

Fridenberg, P.: Teleology and Interpretation of Nystagmus, Ann. Ophth., October, 1908.

Hemmes, G. D.: Hereditary Nystagmus, Ann. d'ocul. **162**:635, 1925.

Herrman, C.: Headshaking with Nystagmus in Infants, Am. J. Dis. Child. **16**: 180 (Sept.) 1918.

Lenoble and Aubineau: Soc. de Neurol. de Paris, January, 1906.
Nettleship, E.: On Some Cases of Hereditary Nystagmus, Tr. Ophth. Soc. U. Kingdom **31**:159, 1911; Roy. Lond. Ophth. Hosp. Rep., 1886-1887, p. 364.
Traquair, H. M.: Clinical Perimetry, St. Louis, C. V. Mosby Company, 1927.
Yawger, N. S.: Familial Head Nystagmus in Four Generations Associated with Ocular Nystagmus, J. A. M. A. **69**:773 (Sept. 8) 1917.

DERMATOSES OF THE REGION OF THE EYE*

CHARLES MALLORY WILLIAMS, M.D.
Attending Physician, New York Skin and Cancer Hospital;
Professor Dermatology, University of Vermont
NEW YORK

This paper is not exhaustive, either in the number of diseases considered or in the description of each disease. It may serve, however, to call the attention of ophthalmologists to some of the common dermatoses that occur in the region of the eye, and to suggest methods for treatment.

DERMATOSES CONSIDERED

Pigmented Nevi.—Pigmented nevi may occur on the eyelids just as on any other part of the body, and they are not generally liable to malignant degeneration. Treatment, therefore, is for cosmetic purposes, and each case must be judged by itself. Whatever is done, treatment should be radical, as nothing is more liable to convert a benign growth into a malignant one than continued or repeated irritation. A few of the pigmented nevi may in time become malignant, and if this occurs, the treatment is the same as that for epithelioma. Some of the pigmented nevi contain hairs, forming the so-called naevus pilosus. If this is the case, the best treatment is to remove the hair first by means of electrolysis, which in itself will destroy a large portion of the nevoid tissue. In many cases this is all the treatment necessary. Vascular nevi in this region require the same treatment as elsewhere, and again the indication for treatment is purely cosmetic. Malignant degeneration of vascular nevi is exceedingly rare. The cases which respond best to treatment are those in which there is a good deal of cavernous tissue, as cure is readily obtained by application of radium. The flat, rather pale, superficial, vascular nevi are not easily treated, as they do not respond readily to radium. If radium is used in large enough dosage to destroy them, a good deal of telangiectasia is usually produced, which may be worse than the original disease.

Impetigo Contagiosa.—Of the infectious dermatoses occurring around the eye, none is more common than impetigo contagiosa. This is a local infection of the skin with one of the pus-producing organisms, usually a streptococcus, and it is exceedingly common as a complication of pediculosis capitis. The earliest lesion is a red spot, which soon

* Submitted for publication, May 14, 1929.
* Read before the Section on Ophthalmology, New York Academy of Medicine, April 15, 1929.

develops a vesicle; this in turn becomes purulent. The pus is thin, and the vesicle or bulla soft and flaccid. As the disease is auto-inoculable, the original lesion is usually surrounded by satellites, and other lesions may appear on any other part of the body as a result of scratching. As the pustules become older, they either rupture and dry, or dry without rupturing, producing a superficial lemon-yellow crust which appears as if stuck on the surface. Removal of the crust reveals a moist base, but no ulceration. The skin between the lesions is normal. The disease is usually readily cured by removal of the crusts and application of from 5 to 10 per cent ointment of ammoniated mercury.

Eczema.—One of the commonest diseases of the face is eczema. The infantile type must be considered first. The condition is well known and needs no description. In infants, the site of predilection is on the cheeks and forehead, and if the case is severe, the eyelids are also involved. In some of the cases the origin may be traced to food sensitization, but there remains a large number in which no adequate cause can be discovered. It has been my experience that patients make the best progress if placed on a diet suitable to their age, or perhaps a little reduced, the food being given at regular intervals, with nothing between feedings except water. At the same time the skin should be treated with soothing applications, among the best of which is Lassar's paste. Protection is the secret of success. The skin should be covered thickly with the ointment or paste and then covered with a mask of gauze. If pruritus is intense, it may be necessary to tie the child's hands and legs in order to prevent scratching and rubbing. In many cases the disease is aggravated by infection of the diseased skin from without, a common cause being coryza either of the patient himself or occurring among his playmates. In adult life, eczema of the face is again common, and in these cases the disease may remain on the eyelids for long periods after the rest of the face is cleared. The eyelids in these cases are swollen, leathery, brownish red, often slightly scaly, and often itch severely. The disease may remain in this condition for a variable period, and then following indiscretion of diet, overexertion or indigestion, or sometimes without apparent cause, it may spread over the face. Treatment is directed to the general condition, any source of irritation without or within, being removed and particular attention being given to the gastro-intestinal tract. Any focus of infection that may be found should be removed and soothing applications, such as calamine lotion, Lassar's paste or an ointment containing oil of cade or coal tar applied locally. Some of these cases may depend on susceptibility to small amounts of arsenic, and in resistant cases, therefore, an examination of the blood should be made for its arsenic content. It is a common experience in hospitals for dermatologic cases to find

patients with severe cases of eczema of the face who improve promptly when put on the hospital regimen, but who relapse as soon as they go home.

Seborrhea and Rosacea.—Two diseases that are nearly related to eczema and that occur frequently in the middle region of the face are seborrhea and rosacea. Seborrhea is an overproduction of sebaceous matter. The sebaceous glands are enlarged, the openings being clearly visible, sometimes patulous and sometimes plugged up with dried secretion. There is always a profuse growth of the bacillus of acne in this sebaceous matter, but whether the bacillus causes the disease is open to question. It seems more probable that the condition is an inherited quality of the skin. The best one can do is to control the symptoms by cleanliness and the use of mild antiseptics. It has seemed to me that cold water applied to the face for ten or fifteen minutes at a time two or three times a day has done more to prevent excessive oiliness than any other procedure.

Rosacea is a patchy inflammatory congestion of the middle of the face, often accompanied by papules and pustules. In contradistinction to acne, it occurs in middle or advanced life, blackheads are not an essential feature, and it depends in some way on the general health, being aggravated greatly by indigestion, especially when accompanied by gastric disturbance. Treatment is directed primarily to the general condition; local treatment is secondary, the best results usually following the use of a soothing application like calamine lotion.

Molluscum Contagiosum.—A disease seen fairly often by the dermatologist is molluscum contagiosum. This is caused by an ultramicroscopic virus, and first appears as a small elevation barely distinguishable from a wart. This gradually increases until it attains a diameter of from 2 to 3 mm., at which stage it has an elevation of about one one half of its diameter. It is then a rounded, pearly, translucent mass. Occasionally, in which case it becomes umbilicated, it attains a slightly greater diameter. As the disease is contagious and autoinoculable, there is usually a group of these lesions on a limited part of the surface. The face, including the eyelids, is one of the favorite sites. The disease is readily cured by the removal of each lesion with a small curet. It is now known, however, that it is not necessary to remove each lesion entirely. Simple pricking with a sharp needle is sufficient. It is important, however, to treat every individual lesion, and as some may be so small as to escape notice, the patient should be seen the second time about two weeks after the first treatment in order that such small lesions may have attained sufficient size to be easily recognized. The disease is superficial, and has neither constitutional symptoms nor sequelae.

Lupus Erythematosus.—Lupus erythematosus occurs characteristically on the face, involving the nose and spreading to the cheeks, whence it obtains the name of the butterfly disease. In this spread, the eyelids are often slightly involved. The etiology is uncertain, but it is now generally believed that the eruption is due to a bacterial toxemia probably of mixed nature, the foci of infection being in some other part of the body. The lesions themselves are dry, sharply outlined, reddish plaques, usually covered with scales, and on removal each scale or crust will be seen to have a number of filiform projections on its lower surface. The surrounding skin is usually normal. As the disease progresses there is usually atrophy in the center, but no deep destruction of tissue. In rare cases, the disease seems to be confined to the eyelids. Until recently, treatment was ineffective, but the introduction of the use of gold and sodium thiosulphate has given a remedy to which the majority of cases yield in a short time.

Lupus Vulgaris.—Lupus vulgaris is a disease which fortunately is rare in this country. It is caused by the lodgment in the skin of tubercle bacilli brought from a focus elsewhere in the body. The earliest lesion is a brownish-red and translucent nodule from 1 to 2 mm. in diameter, usually level with the surface of the skin; it is best described by the common name of apple-jelly nodule. The disease begins in early life. It involves particularly the skin of the face and the mucous membrane of nose and mouth. In the course of years there is usually ulceration and incomplete healing with the production of thick scars which contract producing enormous deformity of the face, including ectropion. In the later stages of the disease, these patients are pathetic objects; the cartilage of the nose is often destroyed, and the entire skin of the face is replaced by irregular scar tissue, this tissue itself again often being the seat of the disease.

Leprosy.—Leprosy is not common in this country except in certain limited regions. Nevertheless, sporadic cases appear in the ports, and one must always be on the lookout for them. One of the earliest symptoms of the nodular type is the appearance of firm masses in the skin in and above the eyebrows. At the same time, similar masses appear in the lobule of the ear. These masses are at first deep in the skin and produce no alteration in the color or texture of the surface. They may go on to ulceration and destruction of tissue. With these, or later, there may also be nodules on the cornea or sclera, resembling closely the nodules produced by tuberculosis. In the early stages, the disease is controlled by the use of chaulmoogra oil, and complete arrest of the process is now reported in many cases.

Syphilis.—Syphilis may attack the eyelids as well as any other part of the skin, but there are only two conditions which here demand atten-

tion. In certain occupations, the lodgment of foreign particles on the conjunctiva is frequent, and it is the habit of the workers to assist each other by the removal of such particles, using for this purpose cloth or paper moistened with saliva. If the donor of the saliva happens to be suffering from mucous patches, there is every probability that the disease will be transmitted in this way to the conjunctiva, producing a chancre. The symptoms of secondary syphilis of the eyelids do not differ from those of syphilis in other parts of the body, and

Fig. 1.—Leprosy.

syphilis on the eye itself is more familiar to the ophthalmologist than to the dermatologist. There is a condition occurring late in the disease which is important, because it may be misinterpreted. Nodular syphilis is usually thought of as an eruption of large ulcerating papules. In some cases, however, the papules are small and resemble closely the inflammatory papules of rosacea. I have seen such a case arching from one eyebrow to the other in which the papules were so small and so soft that at first sight I believed the condition was rosacea, and not syphilis. Closer examination, however, showed that the papules occurred in a fairly continuous line, and within the curve there was distinct though superficial atrophy. The patient at first denied all

knowledge of primary or secondary syphilis, but later recalled having had a sore on the penis two or three years before, which had healed in a few days under the use of simple local applications. Neither he nor the physician whom he had consulted had any idea that it was a chancre. He insisted that he had never observed any secondary syphilis. He recovered promptly under the use of antisyphilitic treatment. This absence of history in cases of tertiary syphilis is of so common occurrence that it is almost the rule.

Alopecia Areata.—In cases of alopecia areata, the eyebrows and even the eyelashes may be lost. If the loss of hair is confined to these

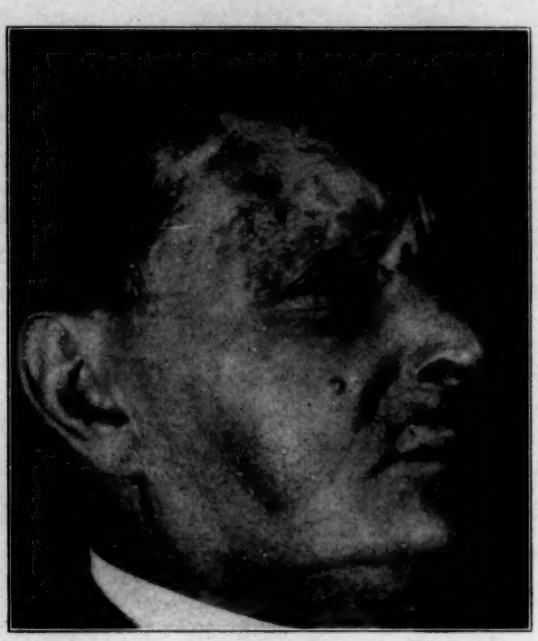


Fig. 2.—Zoster.

parts, the hair on the scalp and the hair on the rest of the body remaining, the prognosis is good, but such cases are seldom seen. As a rule, loss of eyebrows and eyelashes is part of an extensive and severe alopecia areata, in which case the prognosis is bad. The etiology is unknown. Some patients seem to improve after the removal of foci of infection and local treatment with ultraviolet light or crude phenol.

Leukoderma.—Leukoderma may occur on the skin around the eyes as well as on any other part of the body. It is a localized absence of skin pigment producing white patches surrounded by normally colored skin. The cause is unknown, and treatment is worse than useless. Any attempt to restore pigment to white patches by means of stimulation

with drugs or with light is apt to result in increase in pigmentation in the surrounding skin, while the patches remain unaltered, the resulting contrast being more conspicuous than the original disease.

Zoster.—Zoster is of interest to the ophthalmologist when it involves the fifth cranial nerve. There is often a period of more or less indefinite neuralgic pain in the distribution of the nerve, but diagnosis cannot be made until the appearances of the eruption, which is characterized by vesicles occurring in groups in the distribution of the nerve. These vesicles usually become necrotic and heal in the course of from two to four weeks, leaving depressed scars. In some cases the process may stop short of necrosis and heal without scarring. The disease apparently is produced by an infection involving the ganglion

Fig. 3.—Xanthelasma.

of the nerve root and runs a self-limited course. No treatment affects the course of the disease, and the best one can do is to protect the affected region from irritation and infection. The eruption may affect the cornea, in which case scarring may result, leading to a permanent impairment of vision.

Xanthelasma.—Xanthelasma is characterized by sharply outlined chamois-colored plaques in the soft tissue of both eyelids, but is commoner at the inner extremity of the upper lid. The plaques are composed principally of lipids, including cholesterol. They may be flat, thin, irregular and inconspicuous, or thick, raised and of a brighter yellow, so as to constitute a genuine deformity. The diagnosis is easily made, as no other tumor has the same color or is so extensive and at the same time so soft. An allied disease, xanthoma tuberosum multiplex, characterized by tumor-like deposits of lipids, including cholesterol,

may occur on the eyelids, but it is rare in this location, and never occurs here alone, the site of predilection being the elbows and the knees. Xanthelasma is important only from a cosmetic point of view, as there is no danger of malignant degeneration, but the disfigurement is often so great as to demand removal of the tumors, which is best accomplished by monopolar fulguration. Ordinarily this is easily done without anesthesia, the affected skin being lifted from the subcutaneous tissue by a pair of curved forceps. When this is done, the action of the electricity is limited to the skin between and above the forceps and does not extend to the deeper parts.

Xeroderma Pigmentosum.—Xeroderma pigmentosum is best described as premature old age of the skin. It affects the exposed parts,

Fig. 4.—Epithelioma.

that is, the face and hands, and occurs to a limited extent, if at all, on the covered parts of the body. It appears to be due to an abnormal sensitiveness to light. The skin develops brownish patches which become warty, and many of these plaques undergo malignant degeneration. The result is ulceration and superficial destruction of the skin which may lead to perforation of the nostrils and destruction of the eyelids. The disease may be held in check by protection against light and by treatment of the warty epitheliomatous masses with small doses of radium, but the ultimate prognosis is bad.

Senile Keratosis.—Senile keratosis is the name given to the brownish, rough or warty plaques occurring on the skin of the face and hands of old people, and is especially common in blonds. The vast majority of cases never progress beyond the production of these warty masses. A few, however, undergo malignant degeneration; this usually takes

the form of basal cell epithelioma, which fortunately is readily amenable to treatment by means of radium or x-rays.

Epithelioma.—Epithelioma of the face is common, the vast majority of the cases occurring near the canthi, especially the inner canthi. The epitheliomas around the eyes are usually of the basal cell type. The first sign of malignancy is generally the appearance of a small, hard, pearly nodule. As the disease progresses, this nodule increases, often taking the form of a plaque with a depressed center. In time, ulceration appears with a production of adherent crust, the removal of which reveals a shallow ulcer with little discharge. The crust forms again, and the process may go on for years without attracting attention of the patient. This type does not form metastasis; it does not disappear spontaneously, and neglect may lead to serious destruction of skin, cartilage and bone. The cases occurring around the eye are usually best treated by radium, as this gives as good results as any method, leaving little deformity and causing a minimum of discomfort to the patient. It should be remembered, however, that if radium is to be effective, it must be used in large dosage and the result watched carefully. If the condition does not yield in a few months to thorough radiation, the treatment should be stopped and surgical measures substituted.

RETINOCHOROIDITIS JUXTAPAPILLARIS—JENSEN *

S. V. ABRAHAM, M.D.
Staff Resident, Division of Ophthalmology, University of Chicago
CHICAGO

The first report on retinochoroiditis juxtapapillaris was made by Jensen [1] in 1909. In a review of the literature on this subject since that time, I find that thirty-one cases have been described by various authors. More than this number have no doubt been seen and recognized. In a discussion on Verhoeff's paper,[2] there is reference to at least four other cases, making a total of thirty-five.

In his original report, Jensen described four cases that he had observed in a period of ten years in material consisting of about 26,800 cases. One patient, first seen during what was probably the initial attack in 1898, he had under observation for ten years. Recurrences were noted in 1901 and in 1906. Each recurrence showed the site of the infiltration practically unchanged. In the first attack, the whitish, slightly prominent, ovoid, infiltrated area extended nasally from the very border of the optic disk for a distance of about one papillary diameter. The disk margin in the small sector involved was slightly blurred. Below the infiltrate near the nasal border of the disk, the fundus showed the spotted appearance of a chronic retinochoroiditis. The vessels in the region of the infiltrate were not seen. The rest of the fundus was normal. The vitreous showed several threadlike strands extending forward from the region of the posterior pole. The other eye was normal. When the patient was last seen by Jensen, there still remained a single grayish-white opacity in the vitreous, and the fundus showed some irregular marblelike spots with much pigment in an area slightly larger than the site of the old lesions. Examinations of the fields at different times showed practically no change; the fields were characteristic in showing a sector-formed absolute defect extending from the blind spot to the periphery. The macula was not involved. This freedom from involvement of the macula was characteristic of all but one of the reported cases and accounts for the relatively slight visual disturbances noted by the patients. The vitreous floaters seen during the acute attacks would seem to explain the temporary decrease in vision sometimes noted. This usually clears up in one or two months, though slight vitreous opacities may last for many years. After the infiltration had disappeared in his case 1, Jensen noted a slight but definite decrease in the caliber of the arteries in the involved area.

* Submitted for publication, May 20, 1929.

1. Jensen, E.: Retinochoroiditis Juxtapapillaris, Arch. f. Ophth. **69**:41, 1908.

2. Verhoeff: . A Case of Syphilitic Retinochoroiditis Juxtapapillaris, Tr. Am. Ophth. Soc., 1916, p. 14.

The condition affects young adults, favoring neither male or female, and occurs in patients apparently in good general health with no evidence of syphilis, tuberculosis or cardiovascular disease. According to Jensen, there seems to be no tendency toward progression, though Van der Hoeve [3] expressed the belief that the prognosis should be more guarded, as in his case there was involvement of the better eye during one of the recurrences. Groes-Petersen [4] reported that Jensen's oldest patient, when seen two years after the last observation by Jensen, showed a progression of the defect in the field to correspond with the lesion found in the latest recurrence. The condition may last for many years without seriously involving central vision. In case 4 of Jensen the history was suggestive of an onset at the age of 6, twenty-five years before it was first studied.

Lodberg's [5] case, typical in other respects, showed in addition a star-like lesion in the macula resembling renal retinitis. This cleared in four months, leaving only two minute white retinal spots. Vision returned from 5/18 to 5/6.

Gertz [6] described changes in the retinal arteries. The caliber of the arteries in his case were normal, only one disk diameter or more from the site of the lesion. He did not believe, however, that nutritional changes as suggested by Jensen could account for the defect in the field and considered an involvement of the nerve fiber bundle necessary to explain the condition.

Blessig,[7] in 1910, called attention to the discrepancy between the ophthalmoscopic picture and the defect in the field.

Van der Hoeve, agreeing with Groes-Petersen, did not believe that a change in the blood vessels could account for the defect in the field. He modified slightly the theoretical arrangement of the course of the nerve fibers in the retina as presented by von Bunge and Wilbrand-Saenger and concluded that this distribution and an assumption of a neurofibrillitis as the basic pathologic condition best explained the defect in the field.

Dimmer [8] maintained that the condition could not be definitely separated from other forms of retinochoroiditis. The atrophy of the pig-

3. Van der Hoeve: Nervenfaserdefekte bei retinochoroiditis juxtapapillaris, Klin. Monatsbl. f. Augenh. **53**:487, 1914.

4. Groes-Petersen: Retinochoroiditis (Edmund Jensen), Klin. Monatsbl. f. Augenh. **50**:159, 1912.

5. Lodberg: Case Report, Klin. Monatsbl. f. Augenh. **56**:301, 1916.

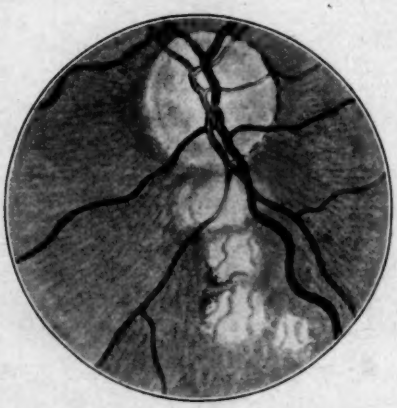
6. Gertz: Case Report, Klin. Monatsbl. f. Augenh. **56**:301, 1916.

7. Blessig: A Case of Retinochoroiditis Juxtapapillaris, Arch. f. Ophth. **74**: 284, 1910.

8. Dimmer: Chorioretinitis Juxtapapillaris, Der Augenspiegel, ed. 3, Vienna, Franz Deuticke, 1921, p. 577.

ment epithelium and, in spots, of the choroid, resembles similar spots in other forms of chorioretinitis. He considered syphilis and tuberculosis as probable causes.

Shertlin [9] believed tuberculosis the chief factor and presented three cases showing iridocyclitis with precipitates on the posterior surface of the cornea. The fundus picture was typical in his case 3 only, though the field showed a rather broad defect, scarcely sector-formed with no tendency to approach the blind spot. In neither case 1 nor case 2 was the fundus picture or the field classically typical. However, in 1911, Groes-Petersen saw the same patient whom Jensen had first seen in 1898, and found an iritis with precipitates on the posterior surface of the cornea.



Four round disk-formed, fawn-colored coalescing areas. The choroidal vessels are visible. The narrower caliber of the retinal artery traversing one of these areas should be noted.

REPORT OF CASE

In January, 1929, C. S., aged 20, a student at the University of Chicago, presented himself for examination with the complaints that his eyes burned, that his lids felt heavy, and that he seemed sleepy much of the time. No history of visual disturbances or of inflammation or injuries of the eyes could be elicited. He had had no children's diseases except smallpox. Six years previously, he had spent six weeks in bed because of an extremely painful sprained ankle, and during this time he had lost about 25 pounds (11.3 Kg.). He had never felt entirely well since that time, although during the past eight months he had regained about 10 pounds (4.5 Kg.). Except for slight though frequent colds, further personal history was entirely negative. The family history was similarly clear of any essential pathologic condition.

On physical examination, the patient was in apparent good health though not robust. He was 6 feet 2 inches (188 cm.) in height and weighed 140 pounds (63.5 Kg.). The results of physical examination were entirely negative.

9. Shertlin: Beitrage zur Retinochoroiditis (Edmund Jensen), Klin. Monatsbl. f. Augenh. **57**:60, 1916.

Roentgenologic examination of the chest revealed no pathologic change in the lungs. Unaided vision was: right eye, 1.2-3; left eye, 1.0-4. With full atropine correction the vision in each eye was brought up to 2.0-4. The right eye was normal, the media and fundus showing no abnormality. The left eye presented a normal anterior segment. With the ophthalmoscope, three short threadlike vitreous opacities could be seen. One fine strand of tissue extended forward from the region just below the disk, almost reaching the lens. Four lesions were seen just below the left disk, as shown in the accompanying illustration. These varied from one-fourth to one-half disk diameter in size; they were round, disk-formed, fawn-colored, showed almost no pigment, and coalesced. All showed spots of choroidal atrophy. Several choroidal vessels were plainly visible. The retinal artery passing over the superior atrophic area was slightly but definitely smaller in caliber than the similar vessels of the surrounding retina, and this was not entirely a contrast phenomenon. The disk itself presented an indistinct margin in its inferior quadrant. Examination with the slit-lamp showed numerous glistening white particles in regular distribution in the anterior vitreous. The fields showed a typical sector-formed defect continuous with the blind spot and a small 1 or 2 degree paracentral scotoma between the blind spot and the fixation point, 7 degrees from the point of fixation.

COMMENT

The underlying pathologic condition of chorioretinitis juxtapapillaris cannot be definitely known until histologic examinations are made. Thus far, no one has made such a report. Verhoeff's case showed clinical manifestations typical of no other reported case; only light perception was present, and examination of the fields was not possible. Histologically, the choroid was involved around the entire disk for an area of about 1 cm., which therefore included the macular region. The retina was extensively involved and showed numerous hemorrhages. This case seems more suggestive of neuritis papulosa peracta (A. Fuchs); this is supported by the history of a primary syphilitic lesion two months before the eye trouble. Verhoeff, himself, questioned the inclusion of his case with those of Jensen, and I have not counted his case in the total of the series here recorded.

While awaiting more information as to the etiology and histologic observations, one therefore can only say that retinochoroiditis juxtapapillaris is a local inflammatory condition of a toxic or infectious nature with involvement of the retinal blood vessels and a small group of nerve fibers in the anterior part of the vagina nervus opticus.

THE RELATIONSHIP OF THE FLAVOBACTERIUM OPHTHALMIAE TO PERIODIC OPHTHALMIA IN HORSES*

ALAN C. WOODS, M.D.
AND
EARL L. BURKY, M.D.
BALTIMORE

Dr. E. C. Rosenow [1] recently described an organism, *Flavobacterium ophthalmiae,* which he believed to be related etiologically to periodic ophthalmia, or moon-blindness, of horses. The specific object in this investigation was to determine if this etiologic relationship of *Flavobacterium ophthalmiae* to the disease could be confirmed.

Periodic ophthalmia, or moon-blindness, is essentially a recurrent serous uveitis, occurring frequently in horses and less frequently in cattle. It affects large numbers of horses in different localities, and almost inevitably results in blindness.

The disease begins with a mild uveal irritation, slight lacrimation and edema of the periorbital fold. The cornea becomes slightly hazy, the pattern of the iris is blurred, the pupil contracts and posterior synechiae form. The aqueous becomes cloudy and then turbid, and exudates appear in the vitreous. The fundus is hyperemic, but frank exudates are rarely found in the choroid and retina. The initial attack lasts a few days and the eye then clears to normal except for such posterior synechiae and vitreous opacities as may have formed. The period of remission lasts for a variable length of time, from a few weeks to several months, when the inflammatory attack recurs. Both eyes are usually affected, but one eye before the other. After several such attacks the inevitable sequelae of uveitis occur, annular and complete posterior synechiae, capsular clouding of the lens, later complete cataract and frequently secondary glaucoma. After a variable period of continued recurrent inflammation, the uveitis finally burns itself out, the intra-ocular tension becomes diminished and some atrophy of the bulb occurs.

The characteristic pathologic changes of the disease, which we have observed in the epidemic studied, will be described in a later communi-

---

* Submitted for publication, June 22, 1929.

* Read before the American Ophthalmological Society, Hot Springs, Va., June 12, 1929.

1. Rosenow, E. C.: Bacteriologic Observations on Periodic Ophthalmia in Horses: Preliminary Report, J. Am. Vet. M. A. **71**:378 (June) 1927; Bacteriologic Studies on the Etiology of Periodic Ophthalmia in the Horse, ibid. **72**:419 (Jan.) 1928.

cation. The pathologic changes heretofore described do not appear characteristic. The most recent description is that of Heinrich Jakob.[2] This author described infiltration and vascularization of the cornea, fibrinous exudate in the anterior chamber, anterior and posterior synechiae, infiltration in the iris and endothelial damage of the vessel walls, which are thickened, dilated and often thrombosed. Detachment of the endothelial and the posterior epithelial layer of the iris is described, with vascularization, exudation and pigment changes in the ciliary body. He also noted thickening and loosening of the choroid with exudations in the perichoroid and perivascular lymph spaces. Degeneration of the retina and swelling and edema of the optic nerve are reported. In the late stages of the disease Jakob described corneal opacities from the endothelial disturbances, pigmentation of the posterior corneal surface and anterior and posterior synechiae, together with atrophy and scar tissue of the iris. The posterior chamber is obliterated; cicatrization and atrophy of the ciliary body and choroid are described, with obliteration of the blood vessels by the thickened walls of the vessels. Detachment and disintegration of the retina may take place. The changes described in the lens are capsular thickening and secondary degenerative changes.

Rosenow's researches may be summarized as follows: Badly contaminated cultures from the conjunctival sacs of three horses were injected intravenously into three rabbits. Two of the rabbits died, but cultures from both the blood and the aqueous showed a small gram-negative bacillus. Using this clue, Rosenow took cultures of the conjunctival sacs of both normal horses and horses affected with periodic ophthalmia. This same organism was found in 10 per cent of the normal horses, in 70 per cent of horses with active periodic ophthalmia and in 30 per cent of horses with quiescent disease. Cultures were also taken of the food and water supplies on the farms on which the disease occurred and on those on which it did not occur. In the fodder of the farms on which there was no disease, the bacillus was found twice, or in 18 per cent of the cultures. It was not found in five specimens of the water supply. On farms on which the disease occurred, the bacillus was found in approximately 50 per cent of all cultures, from both the fodder and the water sources. In four of six attempts the same bacillus was isolated from the turbid aqueous of horses with early periodic ophthalmia.

When the bacillus was isolated from horses, it was usually found with a diplococcus, which Rosenow believed was a mutation form. The bacillus was a yellow pigment-producing, gram-negative, slender rod growing fairly well on ordinary mediums, liquefying gelatin, but not

2. Jakob, Heinrich: Pathologische Anatomie des Auges der Tiere, Ergebn. d. allg. Path. u. path. Anat. **21**:82, 1927.

fermenting indol and not digesting Loeffler's milk. According to Bergey's classification, the organism belongs to the genus *Flavobacterium,* but does not conform in all particulars to any of the numerous varieties described as peculiar to this genus.

Rosenow believed that the organism produced a definite toxin. The organism itself and the filtrate from cultures were alike toxic, and appeared to possess a definite affinity for ocular tissues, the rabbits given intravenous injections showing definite ciliary congestion. A number of rabbits were given intravenous injections of cultures of the bacillus, and the organism was recovered from the aqueous as well as from the liver, spleen and other organs. A picture clinically and pathologically resembling the acute stages of the disease was produced in horses by intra-ocular injection of material obtained from horses' eyes spontaneously affected with the disease. The material inoculated was proved by culture to contain the specific bacillus. Control injections were negative. Pure cultures of the bacillus were injected into the eyes of the two horses. These horses developed what Rosenow believed to be the typical disease, showing exacerbations and remissions. In one horse the opposite, unaffected eye became involved. The condition of the eyes progressed to noticeable atrophy, presumably phthisis bulbi. The bacillus, as might be expected, was recovered from the eyes during the acute phases of the disease.

Rosenow found that the serums of horses that had the disease possessed a definite agglutinating power for the bacillus. Further, he reported that repeated intravenous injections, and repeated introduction into the stomach of filtered and killed cultures of the organism, produced in rabbits a general and ocular immunity to both the bacillus and its toxins.

Rosenow concluded that this bacillus, which he termed *Flavobacterium ophthalmiae,* has etiologic significance in periodic ophthalmia, that the infection is hematogenous, that the portal of entry is the alimentary canal and that the source of the organism is various feeds and water.

A review of Rosenow's report at once recalls the fact that for many years the ocular reaction which follows the intravenous injection of certain bacteria and their filtrates has been well known. In 1911, Guillery[3] described the toxic effect on the eye which followed the intravenous injection of certain pigment-producing and ferment-producing bacteria, such as *B. prodigiosus, B. pyocyaneus* and their filtrates. To the filtrate of such bacteria he gave the name "Uveagifte."

---

3. Guillery, H.: Ueber Fermentwirkung am Auges und ihre Beziehungen zu sympathischen Ophthalmie, Arch. f. Augenh. **68**:242, 1911; ibid. **72**:99, 1912; ibid. **74**:132, 1913; ibid. **76**:226, 1914; Untersuchungen über Uveagifte, ibid. **78**:2, 1914.

This filtrate was at one time studied by one of us (A. C. W.[4]), who concluded that the ocular reaction was only part of the general toxic properties of such material and was in direct relationship to such toxicity. Further, Rosenow's description of the ocular disease produced in horses by the injection of this bacillus does not suggest a true periodic ophthalmia, as observed clinically, as much as it suggests a low-grade uveitis with the usual "ups and downs" of such. On the other hand, the report of the involvement of the second, uninjected eye of one experimental animal commands attention.

EXPERIMENTAL WORK

At the outset of this study, and several times thereafter, Dr. Rosenow furnished us with cultures of the bacillus he had isolated and believed to be related to periodic ophthalmia, and throughout the course of this investigation he gave us all the information requested concerning his work. The organism supplied by Dr. Rosenow had the cultural characteristics described by him, and was proteolytic and nonacid-forming. The organisms we list as "positive cultures" in the following experiments were identical in cultural characteristics and reaction with Dr. Rosenow's bacillus. Occasionally, slight differences were noted in the degree of proteolytic activity, and a few of the organisms showed slight acid production. In five instances, organisms were isolated which were similar in appearance to Dr. Rosenow's bacillus, but differed in that they were not proteolytic and definitely produced acid. In one instance, this organism was isolated from a horse with quiescent periodic ophthalmia, but as these organisms showed cultural characteristics different from those described by Rosenow, the cultures are listed as "negative."

EXPERIMENT 1.—*A. Study of Animals, Food and Water Supply in Farms and Stables Where Active Periodic Ophthalmia Was Present.*—In the spring of 1926, seven cases of periodic ophthalmia suddenly developed on a farm in high, rolling country just outside Baltimore. There were approximately forty horses on this farm continuously. After the first outbreak, no new cases developed. This study was made at this farm, and at an army quartermaster stable in Washington, where there were three horses with periodic ophthalmia and two normal horses.

On the farm where the outbreak of periodic ophthalmia had occurred, cultures were taken from four horses with the active disease. The same technic employed by Dr. Rosenow for taking cultures of the conjunctival sacs was employed. In two of these animals, 50 per cent, positive cultures were obtained. Material from ten normal horses was cultured on this farm. Five of these animals gave positive cultures. Three specimens of fodder and the three different water sources on this farm were cultured. One culture of fodder and one culture from the water

4. Woods, A. C.: Studies on the Actions of Toxins and Protein Degeneration Products on the Eye: II. The Action, Nature, and Source of "Uveal Poison" of Ferment-Producing Bacteria, Arch. Ophth. **45**:451 (Sept.) 1916.

sources gave positive results, an instance of 33 per cent. Cultures were taken of the conjunctival sacs of the three horses with active periodic ophthalmia and of two normal horses in one of the quartermaster stables at Washington. One of the horses with periodic ophthalmia gave a positive culture, all others, both diseased and normal horses, giving negative cultures. Cultures of water sources of this stable were negative.

Summary: Cultures were taken of seven horses with active periodic ophthalmia. Three, or 43 per cent, showed the bacillus described by Rosenow in the conjunctival sacs. Cultures were taken of twelve normal horses, which were kept under the same conditions. Five, or 42 per cent, showed the same bacillus in the conjunctival sacs. Seven cultures of fodder and water were made, two, or 29 per cent, of which gave positive results.

It is interesting that on the farm where seven cases of periodic ophthalmia had spontaneously occurred in 1926, although the organism described by Rosenow as specific in the disease was found widely distrib-

TABLE 1.—*Cultures of Horses, Fodder and Water at Farms and Stables Where Periodic Ophthalmia Was Present*

Source of Material	Number	Positive Cultures	Negative Cultures	Percentage Positive
Affected horses (active disease).....	7	3	4	43
Normal horses	12	5	7	42
Water supply	4	1	3	25
Fodder	3	1	2	33

uted, no other cases of periodic ophthalmia developed during the period of three years that this farm was under observation.

This experiment indicates that there is no difference in the occurrence of this organism in normal and diseased horses on this affected farm.

B. Study of Horses and Water Supply at Farms and Stables Free from Periodic Ophthalmia.—The cultures reported in this experiment were made first on the three farms immediately adjoining the Baltimore County farm on which the outbreak of periodic ophthalmia occurred. There was no periodic ophthalmia, or history of such, on any of these farms. Cultures were taken of sixteen normal horses, two, or 12.5 per cent, of which showed positive cultures. The water supplies on all three of these farms were negative. Cultures were taken of fourteen normal horses at the quartermaster's barn at the Army Medical Center in Washington. There was no periodic ophthalmia in this stable. Six, or 43 per cent, of these normal horses showed positive cultures. Four horses showed an organism, before mentioned, differing from Dr. Rosenow's bacillus only in that it was nonproteolytic and produced acid. These four cultures were classed as negative in the table. An organism exactly similar to this was isolated from a horse with active periodic ophthalmia examined on the farm on which the disease occurred. Water supplies at these farms and stables gave negative cultures.

Summary: Cultures were taken of the eyes of thirty normal horses on farms and in stables free from the disease. Eight horses, or 26 per cent, gave positive cultures. Four normal animals showed an organism somewhat similar. Four water sources gave negative results.

The two experiments described indicate that there is no difference in the occurrence of the organism in normal and affected horses on farms on which periodic ophthalmia exists. The incidence of occurrence of the organism was slightly less on farms on which there was no disease than on farms where periodic ophthalmia was present. No conclusions can be drawn from the studies of the water supplies. Cultures were taken of eight different water sources, four at farms and stables free from disease, and four at farms where the disease existed. The organism was recovered only once. The fodder was studied only on the farms on which the disease was present and only one of three cultures was positive.

EXPERIMENT 2.—*Cultures Taken of Eyes with Periodic Ophthalmia.*—Four horses with periodic ophthalmia were killed. Two had the disease in the stage

TABLE 2.—*Cultures of Horses and Water at Farms and Stables Free from Periodic Ophthalmia*

Source of Material	Number	Positive Cultures	Negative Cultures	Percentage Positive
Normal horses	30	8	22*	26
Water supply	4	0	4	0

* Four of the horses classed as negative showed an organism which was similar, but differed slightly in proteolytic activity and acid production.

of acute exacerbation, the anterior chambers in both being filled with a thick mucopurulent fluid. In these four horses one eye of each was used for culture. These eyes were opened under aseptic precautions and cultures were taken: (*a*) of the purulent aqueous, (*b*) of the vitreous and (*c*) of emulsions of the uveal tract ground up in a sterile mortar with sand. Aerobic and anaerobic cultures were made. The mediums employed were dextrose broth, plain agar, blood agar, cooked meat mediums and Noguchi's rabbit kidney mediums. Independent cultures were made from this material by four different bacteriologists. In no instance, either in aerobic or in anaerobic cultures, in eyes with either active or quiescent disease, was any growth obtained. We were therefore totally unable to corroborate Rosenow's observations that this organism can be recovered from the interior of the eye in horses with either active or quiescent periodic ophthalmia.

EXPERIMENT 3.—*Agglutination of Flavobacterium Ophthalmiae by Normal and Immune Serums.*[5]—Sixteen strains of the bacterium, one the 708 strain furnished by Dr. Rosenow, and fifteen strains isolated from normal horses and horses with periodic ophthalmia, were tested against the serum of a horse which had had repeated attacks of periodic ophthalmia over a period of one year, and against the serum of a normal horse. Both serums agglutinated the organisms up to serum dilutions of 1:20, and not beyond. There was no difference in the aggluti-

5. Captain Reynolds of the United States Army Veterinary Corps cooperated on this phase of the study, and placed at our disposal facilities for this investigation.

native powers of the serum from the horse with periodic ophthalmia and the serum from the normal horse.

Rabbits were given repeated injections of strain 708, and an immune serum was obtained which agglutinated this specific strain up to 1:80. Fourteen strains of *Flavobacterium ophthalmiae* were tested against this rabbit serum.

Agglutination was observed in dilutions from 1:20 to 1:80 in several instances. The agglutination of 1:80 was obtained in two instances, once with an organism isolated from the conjunctival sac of a horse with periodic ophthalmia, and once with an organism isolated from the conjunctival sac of a normal horse.

There is apparently no difference in the agglutinative powers of serums from a normal and an affected horse toward this organism, and no difference in the agglutinative power of an immune serum toward strains isolated from affected and from normal horses.

EXPERIMENT 4.—*Intravenous Injection of Horses with Flavobacterium Ophthalmiae.*—Two normal horses (81 Y 4, and 79 Y 6) were given intravenous injections of 10 cc. of a forty-eight hour broth culture of strain 708. One horse (81 Y 4) showed no reaction. The second horse (79 Y 6) showed malaise and elevation of temperature for thirty hours, and thereafter appeared normal. The eyes showed no abnormalities. The horses were then destroyed, and the eyes removed and sectioned.

Histologic study of these eyes failed to show any lesion. Both the anterior and the posterior ocular segments appeared normal in all sections.

EXPERIMENT 5.—*Intra-Ocular Injection of Flavobacterium Ophthalmiae into Horses.*—Three horses were used in this experiment, two as experimental animals and one as a control. One experimental horse (78 Y 5) was given an injection of 1.5 cc. of a forty-eight hour broth culture of strain 708 in the anterior chamber. The second experimental animal received a similar injection of a forty-eight hour broth culture of a similar organism isolated from a horse with periodic ophthalmia.

Within twenty-four hours, the first horse (78 Y 5) showed clouding of the cornea, hypopyon, iritis, contracted pupil and diminution of the red reflex, associated with lacrimation and photophobia—the picture of a moderate panophthalmitis. The picture lasted about three weeks, the inflammation gradually subsiding. There was no recurrence during four months' observation, at the end of which time the eyes appeared entirely free from inflammation. The animal was then killed, and the eyes were removed for section.

Histologic study showed extremely little. The posterior ocular segment appeared normal. The anterior segment showed a few inflammatory cells over the surfaces of the ciliary processes. At the root of the ciliary process, in one section, was a little round cell infiltration, with possibly slight edema of the ciliary body (fig. 1). Study of the sections gave otherwise negative results.

The second horse (F 210) showed a reaction after twenty-four hours, but of less intensity than that of the first horse. The cornea was clear. There was marked pericorneal congestion, iritis, contracted pupil and posterior synechiae, associated with lacrimation and photophobia. The inflammation subsided rather quickly, and in three weeks the eye was clear. There were no recurrences during four months' observation. The horse was then killed.

Histologic study showed one area of choroidal hemorrhage, with a little old calcification, associated with some edema of the choroid at this point (fig. 2). The posterior ocular segment appeared otherwise normal. The anterior segment

appeared essentially normal. In one area there was, perhaps, an undue number of round cells over the ciliary processes, but the reaction was so slight it was difficult to say that any actual inflammatory reaction existed. In short, evidences of inflammatory reactions in these eyes were extremely slight, and were those which might be expected to follow any nonspecific irritation. The picture did not resemble the pathologic observations noted in eyes with spontaneous periodic ophthalmia.

The third horse (F 867) was used as a control, receiving a similar injection of a forty-eight hour culture of *B. coli* into the anterior chamber. This horse showed the most violent reaction of the three horses. There resulted a purulent

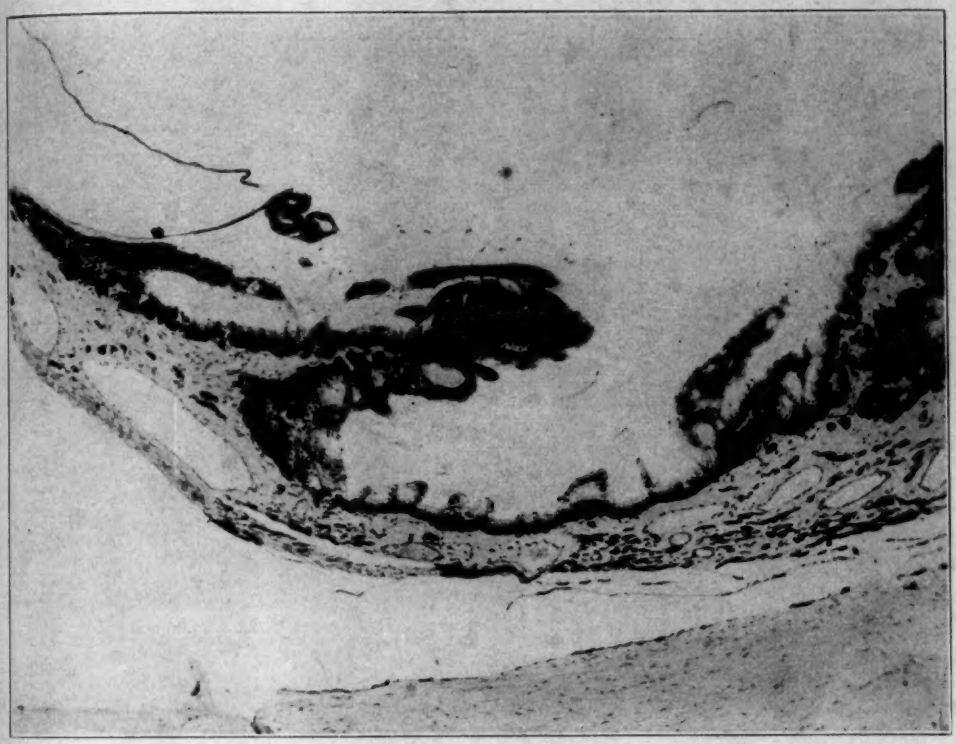


Fig. 1.—Round cell infiltration, with slight edema of the ciliary body.

conjunctivitis, gray cornea, pericorneal congestion and hypopyon. The process continued with slightly decreasing severity for several weeks, the tension became low and the eye began to shrink. The animal then passed from observation and was killed; the eyes were not preserved.

EXPERIMENT 6.—*Intravenous Injection of Living Cultures of B. Prodigiosus, Flavobacterium Ophthalmiae and B. Pyocyaneus.*—Rosenow found that the intravenous injection of *Flavobacterium ophthalmiae* and filtrate of its culture not only was followed by general toxic symptoms, but also produced a circumcorneal inflammation in the eyes of the rabbits into which injections were made. As already mentioned, Rosenow's description and pictures of these ocular reactions coincided with the ocular reaction which follows the intravenous injection of cul-

tures of such proteolytic bacteria as *B. prodigiosus, B. pyocyaneus* and their filtrates. This was originally described in 1911 by Guillery, who believed this ocular reaction was due to the ferments of such bacteria. To this toxic material Guillery applied the term "Uveagifte," or uveal poison. This reaction was later studied by one of us, who concluded that the poison causing the ocular and general reaction was a result of protein degeneration produced in the culture mediums by such bacteria. It seemed probable that the picture observed by Rosenow was identical with this earlier described reaction. Accordingly, a comparative study was made of the reaction caused by the intravenous injection of *Flavobacterium ophthalmiae* and its filtrates, and the reaction caused by *B. prodigiosus, B. pyocyaneus* and their filtrates.

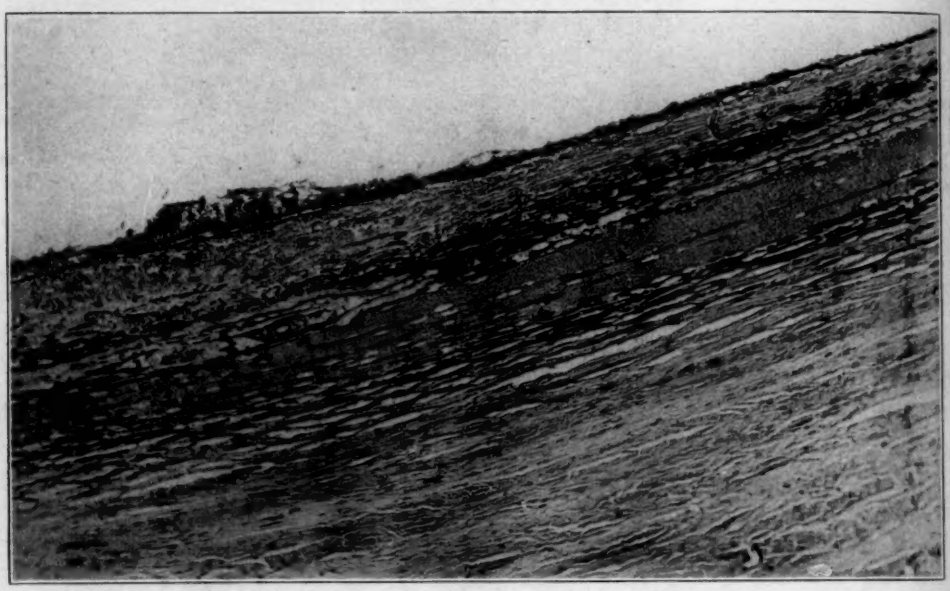


Fig. 2.—Area of choroidal hemorrhage, with a little old calcification, associated with edema of the choroid.

EXPERIMENT 7.—*Intravenous Injections of Living Cultures.*—Rabbits were given intravenous injections of 2 cc. each of twenty-four hour broth cultures of *Flavobacterium ophthalmiae, B. prodigiosus* and *B.pyocyaneus.* There was no general reaction in any of these rabbits. Within two hours each rabbit showed a slight congestion of the nonperforating branches of the ciliary vessels in sheafs above and below the limbus. The reaction was slightly more intense in the rabbit into which injections of *B. prodigiosus* were made. The ocular congestion lasted about twenty hours in the rabbit into which *B. prodigiosus* was injected and about five hours in the rabbits into which injections of *B. pyocyaneus* and *Flavobacterium ophthalmiae* were made. The eyes then cleared and remained normal during the remainder of the life of these rabbits. The rabbits into which injections of *B. prodigiosus* and *B. pyocyaneus* were made died two weeks after the injection, and the rabbit receiving *Flavobacterium ophthalmiae* died eighteen days after the injection. Cultures of the eyes were negative.

EXPERIMENT 8.—Rabbits were given intravenous injections of 4 cc. of twenty-four hour cultures of the same three organisms. The rabbit into which injections of *B. prodigiosus* were made showed a marked pericorneal inflammation within two hours after injection. This reaction had lasted twenty-four hours when the animal died. The rabbit receiving *Flavobacterium ophthalmiae* showed a reaction similar to, but of less intensity than, that in the rabbit into which *B. prodigiosus* was injected. The reaction persisted for almost four days and then gradually faded. The rabbit became thin and drowsy and died six days after injection. The rabbit receiving *B. pyocyaneus* showed only a relatively slight ocular reaction, which lasted about twenty-four hours, and it died two days after injection.

EXPERIMENT 9.—Rabbits were given intravenous injections of 4 cc. of four day broth cultures of *B. prodigiosus, Flavobacterium ophthalmiae* and *B. pyocyaneus.* Within one hour all the rabbits receiving *B. prodigiosus* and *Flavobacterium ophthalmiae* showed marked ciliary congestion. The rabbit into which *B. pyocyaneus* was injected showed moderate pericorneal congestion. No changes were noted in the iris or other ocular tissues. The rabbits all showed marked general reaction. The ocular reactions had persisted without change for five hours when the rabbits were last noted on this day. The next morning all three rabbits were dead.

From this experiment it appears that broth cultures of *B. prodigiosus, Flavobacterium ophthalmiae* and *B. pyocyaneus* all contain a substance which has an irritative action on the ciliary region of the eyes. The cultures were also more or less generally toxic. Old cultures had a greater irritative action on the eyes, and greater toxicity than young cultures. Twenty-four hour cultures possessed relatively little toxicity, the animals dying later of bacteremia. The ocular reactions produced by the cultures of these three organisms were exactly similar in type, were most pronounced in the rabbits receiving *B. prodigiosus,* and were of least intensity in the rabbits into which injections of *B. pyocyaneus* were made.

EXPERIMENT 10.—*Intravenous Injection of Filtrates of Broth Cultures of B. prodigiosus, Flavobacterium ophthalmiae and B. pyocyaneus.*—Six day broth cultures of these three organisms were passed through Berkefeld filters, and the filtrates proved sterile by culture. Rabbits were than injected with varying amounts of these filtrates, with the following results:

A. Filtrate of B. prodigiosus: Three rabbits received intravenous injections, 1, 3 and 5 cc., respectively, of this filtrate. The rabbits receiving 1 cc. of the filtrate showed a moderate pericorneal congestion of the eye, without other ocular or general symptoms. The ocular reaction lasted forty-eight hours, and then subsided. The rabbit appeared normal in every way thereafter. It was kept under observation for three weeks and then used for other purposes.

The rabbit receiving 3 cc. showed a similar marked pericorneal congestion, but without other ocular involvement. There was no general reaction. The ocular reaction persisted for forty-eight hours and then subsided. The rabbit appeared normal in every respect for three weeks; then it was used for other purposes.

The rabbit receiving 5 cc. showed a similar marked circumcorneal congestion, but without evidence of other ocular involvement. There was a definite general reaction, and the rabbit died the day following the intravenous injection.

B. Filtrate of Flavobacterium ophthalmiae: Three rabbits received intravenous injections of 1, 3 and 5 cc., respectively. The rabbit receiving 1 cc. showed a moderate circumcorneal congestion, with no other ocular or general involvement. The ocular congestion persisted for forty-eight hours and then subsided. The rabbit remained normal in every way for three weeks, after which it was used for other purposes.

The rabbit receiving 3 cc. showed a marked circumcorneal congestion, exactly as did the other rabbits. There was also some general reaction, and the rabbit died the day following the injection.

The rabbit receiving 5 cc. showed an exactly similar congestion of the eye, and also a slight general reaction. The ocular reaction persisted for about forty-eight hours and then subsided. The rabbit recovered the day after the injection, and during the three weeks' observation appeared normal as to both the eyes and the general condition.

C. Filtrate of B. pyocyaneus: Three rabbits received intravenous injections of 1, 3 and 5 cc., respectively, of the pyocyaneus filtrate. All the rabbits showed a moderate ciliary congestion, more intense in the rabbit receiving the largest amount of the filtrate. These ocular reactions persisted for about twenty-four hours and then disappeared. No general reaction was observed. The rabbits were kept under observation for three weeks, during which time they appeared normal in every way.

This experiment indicates that the substance occurring in the cultures of these organisms appears also in the filtrates, and has the same irritative action on the ciliary region of the eyes, and the general toxic reaction before noted. There is no essential difference in the ocular and general reaction produced by *Flavobacterium ophthalmiae* and the reactions produced by *B. prodigiosus and B. pyocyaneus,* except that in general the ocular and general reaction produced by cultures of *B. prodigiosus* was more intense, and that produced by *B. pyocyaneus* less intense.

The reactions produced by the filtrates of *Flavobacterium ophthalmiae* appear to be identical with the previously described "Uveagifte" reaction of Guillery, and, like it, are probably due to a protein degeneration product formed in the culture mediums.

CONCLUSIONS

The results of this study indicate to us that *Flavobacterium ophthalmiae,* recently described by Rosenow, has no relationship to periodic ophthalmia in the horse. The organism is one widely distributed in nature. It occurs constantly in the conjunctival sacs of both normal horses and horses with periodic ophthalmia. It appeared slightly more prevalent on the farm where periodic ophthalmia was epidemic than on the farms where periodic ophthalmia was absent, but this difference was not striking.

Cultures of the intra-ocular fluids and emulsion tissues of eyes with both active and quiescent periodic ophthalmia were uniformly negative in our hands, and although *Flavobacterium ophthalmiae* occurs

widely distributed in the conjunctival sacs of both normal horses and horses suffering with periodic ophthalmia, it could not be recovered from the interior of the eye in any instance.

We were unable to demonstrate any agglutinins specific for this bacterium in the blood serums of horses affected with periodic ophthalmia. The intravenous injection of this organism into horses had no effect on the eyes. Intra-ocular injection of the organism produced a moderate secondary uveitis, which did not relapse, and did not appear characteristic of periodic ophthalmia, either clinically or on pathologic study. The sections of these eyes showed only a residuum of slight nonspecific inflammation.

The organism does not produce a toxin in the true sense. Broth cultures of *Flavobacterium ophthalmiae* and filtrates of such cultures produce inflammatory changes in the eye exactly similar to those produced by similar cultures and filtrates of *B. prodigiosus* and *B. pyocyaneus*. This ocular reaction has been studied before and appears to be due to a product of protein degeneration.

We therefore do not believe that *Flavobacterium ophthalmiae* has any etiologic relationship to periodic ophthalmia.

Ophthalmologic Review

AGING OF THE EYE*

AN ABBREVIATED TRANSLATION BY DR. E. E. BLAAUW, OF BUFFALO, OF THE VIEWS OF PROF. A. VOGT AND OF PROF. G. F. ROCHAT

VOGT'S VIEWS†

The life span is a function of the germ-plasm. The end of life is prepared for during senescence. Not all organs show the symptoms of this at the same time. Just as the germ-plasm dictates the duration of the life of the whole organism, so it dictates the duration of the life of the single organ. The study of symptoms of old age shows not only that they are inherited, but also that freedom from them is inherited. The organism is composed of organs and organ parts of varying vitality, long-lived organs and organ parts being present in the same individual side by side with those which are short-lived. This occurrence is related to the idioplasmatic individuality of hereditary signs.

A comparison of man with other mammals shows that senile decline has already begun in the latter at a date when man has not reached a sixth of his life. It follows that in the animal world the senescence of a single organ part is not determined by the absolute number of years, but entirely by the germ predisposition of the species, of the race and of the individual. From time immemorial up to the period of Steinach's experiments, man has tried to find the spring of eternal youth, starting from the false hypothesis that the senium and the physiologic end of life are caused by exogenous factors, such as the loss of hormones or the action of poisons.

Consequently, the physician often tries to prevent these hereditary stigmas. No one will blame him for attempting to forestall, to cure or to minimize such symptoms, although the therapy is ineffective. But he should not permit himself to be misled by appearances, as is the case at present with the so-called medicament-senile-cataract-therapy, nor should he base scientific theories on the apparent achievement of results, for if he does, the road to charlatanism is not far off. Such risks are involved especially with regard to the medical treatment of cataract. In no other condition is it easier to suggest to the patient the possibility of obtaining results, because about ten years are required for a cataract to become ripe, and in most cases it fortunately never develops.

* Submitted for publication, June 12, 1929.

† Vogt, A.: Senile Changes in the Eye. An address delivered before the General Physicians, Schweiz. med. Wchnschr. **59**:301, 1929.

Vision depends on many factors when opacities of the media are present: adaptation to light, size of the pupil, location of the lenticular spokes, and others, as well as on the psychic condition of the patient. Improvement in vision often occurs without any treatment, while on the other hand the condition may remain unchanged for years. Vogt told his patients that they might just as well try to prevent their hair from becoming gray in old age by the application of iodine or other drops as to expect to halt the progress or effect the cure of senile cataract by the use of such treatment. After 60 years of age, 90 per cent of people show senile opacities in the lens; but only a small percentage become blind to an extent that requires operation. One should therefore not speak of "cataract" with beginning opacities. Senile cataract should not be considered without regard to other symptoms of the senium of the organism.

Various diseases can, of course, produce clinical pictures similar to those of natural senile decline. Grayness of the hair or baldness can originate through external influences as well as through heredity, but this fact should never be taken as a reason for confusing either of these totally fundamental causes with the other, not even when, as is occasionally the case, they act together and can scarcely be separated. Slit-lamp microscopy furnishes a possible method of separating morphologically senile and exogenous changes. The exogenous cataract, which is caused by inner secretorial disturbances, diabetes, poisoning, serious disease of the eyeball, ultra-red rays, etc., differs at the very outset from senile cataract.

With advancing age, the eye shows signs of senility in all its parts: The conjunctiva tears more easily and ectasias of its vessels appear; the pingueculae proliferate; the limbal vessels are obliterated; the arcus senilis becomes prominent (a preeminently hereditary symptom); the opacity of the cornea increases; senile warts form on Descemet's membrane; the pupillary pigment zone resolves, and its pigment scatters on the posterior surface of the cornea; the retinal pigment zone shows holes, and the sphincter becomes smaller and the pupil more rigid. A distinctly hereditary type of cataract appears; the vitreous shows senile decline, and its fibers condense into points and opacities. The following important changes are found in the retina: presenile and senile macular degeneration in a definitely hereditary form, peripheric-chorioidal atrophy of the retina with cystoid cavities and reactive pigment proliferation, colloid bodies of the hyaline membrane, senile sclerosis of the macular-choroidal vessels, circumpapillary chorioidal atrophy and increased rigidity of the sclera. A single sense organ, in fact produces sufficient examples of degeneration to demonstrate the futility of the attempts to explain the senium by exogenous factors. Length of life is a biologic hereditary

symptom; an average duration is therefore normal. All characteristic senile symptoms are biologic symptoms and, accordingly, the postponement of senile decline is only an extreme variant in one direction of a biologic symptom.

ROCHAT'S VIEWS†

The patients were old and were dissatisfied with their conditions. The first, a well preserved man, aged 60, with barely 1/10 vision, on account of senile cataract could no longer read, even with his spectacles (+3.5). He was willing to follow the advice of his medical advisers, but as he was free from prejudices and if the physicians maintained that nothing could be done, he was inclined to try any form of quackery or "wonder cure" that presented itself.

Senile cataract should not be considered as originating during or because of old age. Many patients do not show any signs of general decline due to age. The slit-lamp has demonstrated that a senile cataract really begins in youth. At the age of 20, coronary cataract is often found. It is therefore more correct to speak of a congenital tendency toward early degeneration of the lens than of a condition caused by the age of the body. This implies that external causes, such as the intensity of light and heat, can have no important bearing on the condition. It does not mean, however, that such influences are not able to hasten the process of impairment in persons who are predisposed to it by heredity; young persons with a distinct coronary cataract should therefore not be exposed to these conditions—they should not become glassblowers or assistants in x-ray establishments. If they have to deal with ultraviolet rays, they should use spectacles, even if the effect of these rays is still a moot question.

The patient under observation has not been helped by treatment. He had heard that his cataract was not yet "ripe," and that he had to wait, etc.

Formerly a sine qua non, this condition of "ripeness" is no longer considered necessary, thanks to the improved technic of operation. The thorough use of local anesthesia and the immobilization of the eye enable the surgeon to disregard the general behavior of the patient and permit the complete removal of an extremely unripe cataract. With the added use of artificial light and better antisepsis, it is unnecessary for patients to wait for better conditions in the eye itself. There are, however, drawbacks to early operation. Greater skill and operative experience are required on the part of the surgeon. The eye operated on is irritated longer, and the extent of ultimate vision is somewhat less than when the lens is ripe; possibly an iridectomy is necessary.

---

† Rochat, G. F.: Senile Changes in the Eye. An address delivered at a clinic for students, Nederl. Tijdschr. v. Geneesk. **2**:1340, 1929.

The question arises as to how to bridge the period of waiting. Steinach and Voronoff have demonstrated that the different age symptoms are not so incapable of being influenced as was formerly supposed, and that the search for internal treatment for cataract should not be rejected. Römer's lens preparation (1907), which hypothetically should bind the cytotoxins endangering the lens, is entirely forgotten, as are also Davis' (1922) lens-antigen-treatment and other similiar methods. Iodine given in drops, subconjunctivally or internally, has been recommended and employed extensively. Angelucci used iodophoresis with iodine and claimed important improvement of the vision and of the objective condition of the lenses.

All of these measures have, in general, dubious success. Does this mean that they should never be employed? It was Uhthoff's opinion, for instance, that every medical treatment was useless and expensive for the patient and gave him false hope. Some Dutch ophthalmologists think likewise. Rochat did not agree with this. He felt that these men do not consider the patient's condition sufficiently and what it means to him to wait so long with the secret idea that something could be done, an idea which ultimately drives him to the quack. Rochat considers it important for the patient to feel that the physician takes a real interest in him, and when he (Rochat) considers that the patient should not be operated on, he gives him potassium iodide, for the use of which a scientific background exists. Van der Hoeve, for example, has found that it counteracts the swelling of the lens vesicles; it is, besides, easily taken and innocuous.

The patient in question is told to take the drug internally, to use it as drops, and to report after two months; he is also told that an operation in the future will be necessary, but that the time for it cannot be decided on at present.

After the patient has been dismissed, perhaps it will be considered that his problem is solved and that nothing valuable has been accomplished. This view is a mistake. It is an important part of the physician's function to comfort the patient and to sustain his courage by an expression of interest in his case.

The second patient, aged 82, for the past few years had read less easily. Various oculists had tried in vain to help him. He thought that they had not shown sufficient interest, as he claimed that he could see well at a distance. The lens and refractive media were sufficiently clear, but he recognized small objects only when they were moved in the paramacular field. He had central scotoma for colors and an irregular granular change of the yellow spot. The only encouragement that could be given him was that the degeneration would remain limited to the yellow spot, and that he would not become totally blind.

CONCLUSION

Patients exhibit symptoms of age in the vessels of the eye with frequent hemorrhages, vascular obliterations and degenerations through vascular sclerosis. Further than this, there is no local disease of the eye, unless patients show other important bodily changes.

Rochat limited himself to the demonstration of the foregoing two cases, because they typify the symptoms that are ordinarily the only ones appearing in otherwise healthy persons which trouble them seriously.

Miscellany

REPRODUCTION OF PHOTOMICROGRAPHS

The reproduction of photomicrographs in this journal is limited by the available space on the page.

The column width is 4¼ inches. All cuts have a ⅛ inch shoulder on each side to permit of the metal being fastened to the wood block; hence, if consistent with the material to be shown, illustrations are reduced to column width—that is, to 4 inches. Larger cuts not only cost more but necessitate additional expense in arranging makeup. When necessary or especially desirable, larger reproductions can be produced, but only in very exceptional instances are cuts made more than 5½ inches wide.

When photomicrographs more than 5½ inches wide are submitted, authors should decide whether they prefer to have only the significant portion of the illustration reproduced full size or to have the entire picture shown with reduction. Notation of the choice should accompany the manuscript; in case choice is not indicated, manuscript editors will use their own judgment as to the procedure to be followed.

Abstracts from Current Literature

EDITED BY DR. WILLIAM ZENTMAYER

Physiology

THE FUNCTION OF THE SINGLE ELEMENTS OF THE RODS AND CONES IN THE VISUAL ACT. L. MAGGIORE, Ann. di ottal. e clin. ocul. **57**:389 (April-May) 1929.

The author discusses the various theories of vision, especially as regards the exact location of the visual function. While agreeing with Fortin that the cone is too large to function as the element in the reception of visual stimuli, he does not believe it necessary to consider this element, as Fortin does, to be localized in the layer of nerve fibers. Anatomic studies of the retina fixed by various methods indicate that only the internal segments of the rods and cones are suitably arranged for the reception of stimuli in accordance with what we knew of the visual function. Calculations from the *minimum separabile* show that the space which separates retinal receptors at the fovea must be only from 0.004 to 0.005 mm. Anatomic studies of the retina show that the external segments of the rods and cones besides being larger than this, are arranged with an undulating external surface, their processes extending into the pigment layer and being separated by processes of the pigmented cells. The internal segments, on the other hand, are regularly bounded by the internal limiting membrane, and form a perfectly regular mosaic with elements of a size compatible with the *minimum separabile*. Hence the author believes that these internal segments must be considered the receptor organs of visual stimuli, the external segments, by their relations with the pigment epithelium, probably serving in some way to prepare them or sensitize them to such impressions.

SANFORD GIFFORD.

THE INFLUENCE OF THE SYMPATHETIC NERVE ON THE PROTEIN CONTENT OF AQUEOUS. H. K. MULLER and R. PFLEINLIN, Arch. f. Augenh. **100-101**:91, 1929.

Using the nephelometric method, the authors found that the protein content of rabbit's aqueous averaged 0.04 per cent. Deviations occurred from animal to animal and also between the two eyes of the same animal.

With the animal under an anesthetic and cutting the cervical sympathetic on one side, they could find no constant difference in the protein content of the two eyes one hour later. Since this was contrary to the reports of most investigators who found a marked increase in the protein on the side of section, they repeated the experiments using ether anesthesia. This resulted in an increase in protein on the side of the section.

They next repeated the same experiments using no anesthetic, but hypnosis, which they state (without describing in detail) is easily carried out on rabbits. A small but inconstant increase in the protein on the side on which the operation was performed was the result. A further series was undertaken under hypnosis but allowing a longer interval to elapse after the section of the nerve before withdrawing the aqueous. This showed no demonstrable difference due to the time interval which elapsed up to twenty-four hours.

Electrical stimulation of the cut sympathetic caused no change in the protein content of the primary aqueous. They found that section of the nerve in itself caused an increase in protein content of the aqueous of second formation, and electrical faradization of the nerve was found to diminish this somewhat.

FRANCIS HEED ADLER.

Vision

PHOTOMICROGRAPHY OF THE LIVING EYE: V. THE PHYSICS OF CERTAIN TYPES OF CORNEAL OPACITY. L. D. REDWAY, Am. J. Ophth. **12**:286 (April) 1929.

This report is concerned with the behavior of diffuse generalized corneal opacities under light of different wave lengths, and with variations of visual acuity in the presence of such opacities under light of known wave length. The experiments are based on photomicrographs of eyes with diffusely clouded corneas taken by white arc-light and also through a Wratten F-filter cutting at 6,100 millimicrons. Photographs were also taken through partially opaque or ground glass. Determinations were likewise made at 32 feet with the naked eye and with the same filters that were used in the photographic tests. The author draws the following conclusions: 1. The visual acuity of eyes presenting opacities of a general diffuse order may be improved over the best that can be obtained with correction of refractive errors and by white light, by excluding light of wave length less than 5,100 millimicrons, and under conditions of ordinary illumination. 2. It is useless to attempt to gain greater resolving power by utilizing frequencies beyond 5,800 millimicrons, no matter what the order of opacity may be, since not only does retinal sensitivity decrease rapidly beyond this point, but contrast is so exaggerated as to be practically intolerable.

W. S. REESE.

Experimental Pathology

ACUTE PIGMENTARY DEGENERATION OF THE RETINA AFTER POISONING WITH PREGLE'S SOLUTION CONCENTRATED × 10. W. RIEHM, Arch. f. Augenh. **100-101**:872, 1929.

The report of a number of cases of poisoning after the use of Pregle's solution (septojod) has recently been published. The author succeeded in producing similar changes in the eyegrounds of rabbits by injecting this drug intravenously.

Septojod is a concentrated Pregle's solution. The latter drug has been used extensively in all fields of medicine and surgery. It consists of a watery solution isotonic with body fluids containing about 0.04 per cent free iodine together with a large quantity of bound iodine. In the presence of weak acids, such as occur at the site of bacterial infections, the bound iodine is released as nascent iodine and exerts its full antiseptic action. Because of the volume necessary to inject in cases of septicemia, a concentrated solution septojod has appeared on the market. The use of this is not without some danger to the eyes, and the author reports three cases which he personally observed, in which an acute pigmentary degeneration of the retina occurred. All three cases were in women with puerperal sepsis. Vision was reduced to light perception within twenty-four hours. The pigment epithelium was chiefly affected, and the eyegrounds resembled those of typical pigmentary degeneration with most of the pathologic condition located at the posterior pole. The blood vessels showed no changes.

Experiments on rabbits demonstrated that 1.5 cc. per kilogram of body weight produced definite changes in the eyegrounds of nonalbino rabbits, similar to the clinical picture. The animals suffered no other demonstrable pathologic changes; so the author concludes that this drug exerts a specific toxic action on the retina.

FRANCIS HEED ADLER.

DEMONSTRATION OF VITAMIN A IN RETINAL TISSUE AND A COMPARISON WITH THE VITAMIN CONTENT OF BRAIN TISSUE. EJLER HOLM, Acta Ophth. **7**:146, 1929.

A group of albino and brown rats were fed on a basal diet free from vitamin A. When the animals began to lose in weight and xerophthalmic ocular symptoms

— narrow eye slits, brownish secretion and keratitis — occurred, their ration was supplemented by retinal tissue, gray or white brain tissue or butter fat. The experiments described in this paper tend to show that brain tissue — white or gray — is poor in vitamin A and that retinal tissue possesses a considerable amount, for a distinct effect is produced with as small a dose as 0.05 Gm. of tissue. A daily dose of 0.35 Gm. added to the experimental diet is insufficient, however, to induce optimal growth in the rat, but 0.75 Gm. will increase the growth curve. This amount of retinal tissue corresponds to from 0.08 to 0.10 Gm. of dry substance. The author believes, therefore, that the retina belongs to the parts of the body that are comparatively rich in vitamin A. A daily dose of 0.30 Gm. of butter fat which was used in control animals did not give as good results as the maximum amount of retinal tissue.

From the observations made by other investigators, that the vitamin factor is usually attached to the lipoids and that lipoids are found in the outer segments of the rods and that visual purple is localized in the same area, he concludes that vitamin A and visual purple may be associated in the same way as vitamin A and lipochromous pigments in other parts of the body. If this is so, the A factor is present in the retinal tissue in a highly concentrated form.

A. M. YUDKIN.

Lids

PTOSIS OPERATION ACCORDING TO THE SHOEMAKER METHOD. H. W. SCARLETT, Am. J. Ophth. **11**:779 (Nov.) 1928.

The operation described is a modification of that suggested by Parinaud of stitching the whole tendon of the superior rectus muscle to the lid. As done by Parinaud, the stitches were brought up between the tarsus and the orbicularis muscle and carried out at the ciliary margin in front of the eyelashes. The method employed by the author was as follows: The upper lid was everted and the superior rectus tendon isolated but not severed from its attachment. A double-armed suture was next inserted in the middle third of the exposed tendon from within outward, the loop next to the eyeball. The long ends of the suture were then wrapped in gauze and laid aside. An incision was then made the entire length of the lid through the skin and orbicularis muscle parallel to the upper border of the tarsus. The upper border of the tarsus was freed of the orbicularis; through the opening thus made, the tendon sutures were drawn and a bite was taken in the middle third of the upper portion of the tarsus proceeding through the orbicularis muscle and coming out on the skin surface where the ends were tied over a small piece of rubber tubing. The knot was tightened to overcorrect in order to maintain the proper after-position of the lid. The result at the end of six months was excellent as to position of the lid and movements of the eyeball in all directions.

W. ZENTMAYER.

PIGMENTATION OF ROOTS OF CILIA CAUSED BY ACARUS DEMODEX FOLLICULORUM. F. B. BLACKMAR, Am. J. Ophth. **12**:373 (May) 1929.

For several years, the author has been interested in pigmentation of the roots of the cilia of the eyelids and considers it a not uncommon condition. The patient complains of itching of the lid margins, with an intense desire to extract the cilia. The upper lid is affected more frequently, the condition usually starting at the outer canthus. By careful examination with the loupe, a black deposit can be seen

in the skin around the cilium. In two cases, the author has been able to demonstrate the infecting agents alive on the shafts of extracted cilia. Treatment does not seem effective from the curative standpoint. W. S. REESE.

Conjunctiva

TREATMENT OF RECURRENT PTERYGIUM. M. WIENER, Am. J. Ophth. **11**:876 (Nov.) 1928.

The author mentions the various procedures that have been advocated for the treatment for pterygium and states that no matter what method is used recurrences will occasionally take place. For the cure of this condition he advises the use of exceedingly thin epithelial grafts. A clean dissection of the growth is made including a margin of the apparently clean cornea for a distance of at least 1 or 2 mm. After getting under Bowman's membrane an effort should be made to remain on the same corneal layer in the dissection. The dissection is continued beyond the sclerocorneal margin including the base, and the pterygium is excised beyond the scleral margin. It is essential to undermine and loosen it as well as the normal conjunctiva above and below. The graft is placed on the globe and slid under the undermined conjunctival edge for a distance of 4 or 5 mm. He states that he has often removed the graft at least six months or a year after its placement without fostering recurrence of the pterygium. W. ZENTMAYER.

Trachoma

IS THE BACTERIUM GRANULOSIS OF NOGUCHI THE CAUSE OF TRACHOMA? K. LINDNER, Graefe's Arch. f. Ophth. **122**:391, 1929.

At the invitation of Dr. Proctor the author visited the Rockefeller Institute in New York where he saw the monkeys Noguchi had injected with *Bacterium granulosis,* and then spent some time in the Indian Reservations in New Mexico where he studied the type of trachoma found there. The present paper deals with his conclusions drawn from these studies.

He is convinced from an examination of the injected monkeys that they do not present the clinical picture of trachoma. All the animals he saw were typical cases of conjunctival folliculosis. The conjunctiva in all cases was transparent and of normal thickness, even though follicles were present. There was not the slightest trace of papillary hypertrophy or any significant thickening of the conjunctiva. The eyes showed no secretion and little if any injection. Such a typical cleancut picture of a pure folliculosis is seldom seen in man.

In the Indian school in Albuquerque the author studied the types of trachoma commonly met with. Following the classification of MacCallan he divides the cases into four stages: (1) before a clinical diagnosis can be made with certainty; (2) fully developed trachoma with no scar formation; (3) visible scars present but the surrounding conjunctiva is not yet diseased, and (4) healed end-stages of scar formation.

Of the cases examined a large proportion were typical trachoma and showed the Prowazek inclusion bodies and initial bodies.

An examination was then made of three of four cases from which Noguchi isolated *Bacillus granulosis.* Of these, case 1 showed no signs of trachoma. The conjunctiva was completely normal and no scars remained. Cases 2 and 3 showed the signs of a definite trachoma in stage three.

Lindner then describes the difficulties attendant on making a diagnosis of true trachoma, and points out that folliculosis is a disease of the adenoid tissue in the

conjunctiva and the epithelial layer remains normal whereas in trachoma the infection is primarily in the epithelial layers, and always leads to papillary hypertrophy of the tarsal conjunctiva.

He takes exception to Elschnig's point of view, who groups trachoma and folliculosis together, and insists that they are etiologically entirely separate.

He further points out that the monkeys used by Noguchi, i. e., *Macacus*, have been found by nearly all experimenters to be highly resistant to takes from injection of trachomatous material, whereas Noguchi failed to infect orang-utans which have previously been found best suited for this purpose.

He believes that Noguchi has not isolated the cause of trachoma, but that *Bacterium granulosis* is the cause (or one of several) of folliculosis.

FRANCIS HEED ADLER.

Cornea and Sclera

EXPERIMENTAL TUBERCULOSIS OF THE CORNEA. P. EMANUELE, Ann. di ottal. e clin. ocul. **57**:314 (April-May) 1929.

Previous work on the subject is reviewed. The author used rabbits in his work, inoculating living and killed human tubercle bacilli by scarification and by intracorneal injection, and also injecting organisms into the blood stream and into the anterior chamber. Following inoculations in the cornea, lesions developed after from seven to ten days, which went on to caseation, followed by elimination of the caseous material after from two to three months. Tubercle bacilli could be found on section but only in the lesions, which showed no tendency to extend into the surrounding cornea. Descemet's membrane was resistant to the process, and perforation never occurred. The iris showed hyperemia with the formation of small grayish nodules which were more numerous when inoculation was made near the limbus. The nodules disappeared as the corneal lesion healed. The other ocular structures were never involved. Inoculations into the blood stream never caused corneal or other ocular lesions. Since the bacilli showed no tendency to invade the surrounding cornea, the corneal and iridic lesions must be attributed to their toxins. (Bibliography and photomicrographs.)

SANFORD GIFFORD.

A CASE OF KERATOCONUS OF ENDOCRINE ORGIN CORRECTED BY PLURIGLANULAR OPOTHERAPY. W. MEERHOF, A. MEERHOF and J. MONTES PAREJA, Arch. de oftal. de Buenos Aires **4**:129 (March) 1929.

After calling attention to the obscure etiology of keratoconus the authors refer to Siegrist as the first to study the problem from an endocrinal point of view. This, although at times referred to, together with other possible etiologic factors, has not received any sanction, the treatment recommended being mostly surgical or by means of optical correction with contact lenses.

During the last year, the authors have searched for endocrine disturbances in all the cases of keratoconus they had at hand, seven in number, having been able to find evidence of disturbance of these functions in all. During these investigations, they were fortunate in being able to observe one case in its initial stage, in which the therapeutic result of treatment, carried out in accordance with these views, gave them a full confirmation.

The case was that of an Uruguayan boy, aged 14, who, up to the eighth year, had presented a normal physical and mental development. After vaccination against typhoid, he began to hold his reading matter extremely close to his face and at the same time to grow extremely fat. There were no hereditary or personal ante-

cedents, except a constant change of glasses. His sight in the right eye was 1/12, in the left 1/15; a conical deformation of the cornea was observable with the ophthalmometer and in skiascopy, and with the slit lamp a slight thinning of the corneal center. A general examination showed a monstruous adiposity, most pronounced in the pectoral, gluteal, femoral and inferior abdominal regions with atrophy of the genital organs and absence of the secondary sexual features. There were no signs of intracranial hypertension, nor of compression of the optic pathways, nor of any hypophyseal hypertrophy, the sella being small in size. Psychically the patient presented infantile characteristics, the case readily falling into the class of adipogenital dystropies (Fröhlich) with mental puerility. The Goetsch test was negative; the cardio-ocular reflex was exaggerated, the pulse falling from 102 to 68; Parisot and Richard's sign was negative. Slosse's sign was normal, Ascoli and Fagucoli's pituitrin test was undecided, in the Claude Bernard and Piedelierce test the arterial pressure fell 10 mm. in sixteen minutes, with an unchanged pulse rate and without traces of sugar in the urine; there was a 10,000 leukocytosis; the basal metabolism (Sanborn-Benedict) was—2 per cent; hydrocarbon tolerance was high; the thermoreaction test was negative; the injection of 2 Gm. of fresh testicular extract caused a marked slowing of the pulse but not so pronounced as that produced by the compression of the eye. His teeth were irregular but without any syphilitic stigmas. The neurologic examination was negative. There was an apex Potinian murmur and a globular heart. Emotions produced red plaques in the skin of the boy's chest. The Wassermann reaction was negative.

The patient was subjected to an opotherapic pluriglandular treatment, which was carefully watched every day, his tolerance being measured by the different tests.

A progressive general and local improvement followed; in eight months there was a reduction in weight of 17.75 Kg., with improvement in the psychical and mental conditions, the eyesight in both eyes reaching 1/3 in the right and 1/4 in the left.

C. E. Finlay.

The Etiology of Keratoconus. A. Loewenstein, Arch. f. Ophth. **121**:736 (March) 1929.

The author reports a case of unilateral keratoconus (right eye) which developed immediately after the removal of an enormous intrathoracic goiter on the right side. The patient was a woman, aged 48, who had been under the observation of several ophthalmologists. The last examination three months before the operation for goiter showed normal visual acuity in each eye (with a small minus glass). The diagnosis of keratoconus was made eight weeks after the operation. During the following thirteen years, the patient was seen by many ophthalmologists, all of whom found the unilateral keratoconus. The other eye was finally operated on for cataract, and normal vision was obtained. Thirteen years after the operation for goiter the palpebral fissure and the pupil were slightly wider on the right side than on the left. Cocaine dilated the left pupil but not the right. The right cornea was slightly hyperesthetic. The right cornea bulged in the shape of a central conus, with slight thinning of the apex. A few deep opacities were present in the apical parts of the conus. No ring of Fleischer was found.

The author believes that the disturbance of the equilibrium of the endocrine glands combined with a lesion of the right sympathetic nerve is most likely the cause of the unilateral keratoconus. Experiments on rabbits (extirpation of the ganglion supremum, the thyroid and the parathyroids on one side) showed all the well known changes which follow extirpation of the sympathetic nerve. The

iris of the side operated on changed color, becoming considerably lighter. The cornea did not show any changes in curvature, thickness and condition of the surface. Further experiments will be carried out on dogs and cats.

It seems likely that the sympathetic nerve plays an important rôle in the nutrition of the cornea. The basal metabolism could not be measured in Loewenstein's case because the patient wore a tracheal cannula continuously which could not be connected with the respiration apparatus.

-KRONFELD.

ON THE SUBSTRATUM OF THE PIGMENT RING OF DESCEMET'S MEMBRANE IN PSEUDOSCLEROSIS. A. VOGT, Klin. Monatsbl. f. Augenh. **82**:433 (April) 1929.

The pigment ring of Descemet's membrane was described first by B. Kayser in 1902. He brought it in connection with a general disease, supposedly multiple sclerosis. Later it proved to be pseudosclerosis. Reports of three similar cases were published by B. Fleischer and Salus soon afterward. The origin of the pigment remained mysterious. It did not originate from the blood or bile.

Reviewing the literature Vogt shows that the pigment ring has been observed in pseudosclerosis only and is characteristic for this disease. This progressive degenerative process consists of a peculiar type of cirrhosis of the liver, and degenerations of the lenticular nucleus (striated body, thalamus, subthalamic region). It is similar to, or perhaps identical with, Wilson's disease, described in 1912. The origin of the pigment has been cleared according to Vogt. The most important publication is that of Rumpel (*Deutsche Ztschr. f. Nervenh.* **49**:54, 1913). It is based on the research done by Soeldner who found silver, antimony and copper in the liver, kidneys and in the pigment. The silver is soluble in cyanide of potassium. No arsenic was found. The liver, kidneys and other organs store away certain metals which enter the body with the food. This condition may lead to insufficiency of the liver, to changes of the metabolism and to the physical, psychical and neurologic symptoms related to pseudosclerosis, perhaps also to those of diabetes and argyrosis.

H. Spatz (*Ztschr. f. d. ges. Neurol. u. Psychiat.* **77**:261, 1922) proved that the corpus striatum, especially the globus pallidus and the substantia nigra, shows special activity in the iron metabolism. He supports the thesis of Siemering and Oloff that these organs are endowed with a particular chemical activity (*Klin. Wchnschr.* **1**:1087, 1922).

Vogt reports three cases of pseudosclerosis presenting the same picture of the region of Descemet's membrane in both eyes. The colors resembled those obtained by artificial impregnation of the cornea with colloidal silver. This observation, in the author's mind, proves that the pigment ring in pseudosclerosis is produced by silver. Microscopic examination of an eye of one of these patients who died later and chemical experiments with cyanide of potassium supported his opinion. Weinland, furthermore, found silver in a piece of the kidney of the same patient. Vogt disagrees with Fleischer and Hall (La dégéneration hepato-lenticulaire, Paris, Masson & Cie, 1921), who do not think that the pigment ring is produced by silver, and with Kubik, Hessberg and Jess who consider urobilin as its cause.

Another point remained to be cleared; the similarity between the cataract coupled with the pigment ring in pseudosclerosis, and that produced by copper in the anterior lens capsule (so-called sunflower cataract). Two of Vogt's patients presented cataracts of the sunflower type, as seen in the slit-lamp pictures appended. The history of one of them, a woman, aged 60, shows that the ring had been observed for forty years, since 1888. She had received about 6 Gm. of silver nitrate at that time, which is about one eighth of the dose considered necessary

to produce argyrosis. She had never received copper therapeutically. The cataract, in all appearance, was caused by copper stored away in the liver. The color scheme of the pigmented ring in pseudosclerosis, seen by means of the slit-lamp, is brown, yellow, green, ultramarine-blue. It resembles the color scheme of colloidal silver albumin to such an extent that the pigment in pseudosclerosis must be considered identical with these silver combinations.

K. L. STOLL.

THE FIRMNESS OF THE CORNEA AND THE MARGINAL RING OF SCHWALBE. A. FUCHS, Ztschr. f. Augenh. **67**:129, 1929.

The firmness of the cornea is afforded by the sturdiness of the bundles of connective tissue, the elastic elements and Descemet's membrane. The center of the cornea is thin and the periphery much thicker. The cornea has an anterior and posterior reinforcement tissue. The latter is well constructed, and the circular bundles making up this reinforcement lie in the inner aspect of the inner portion of the sclera. The anterior ring of connective tissue is known as Schwalbe's ring. This tissue is not present in all eyes. In some eyes it is powerful and in others, feeble. A well developed Schwalbe's ring is found in a small percentage of human eyes.

A. M. YUDKIN.

Lens

SPONTANEOUS RESORPTION OF JUVENILE CATARACT. FERRER, Am. J. Ophth. **11**:886 (Nov.) 1928.

After a brief review of the literature, the author reports his own case, that of a negro, aged 16. At about the age of 13, the vision of the right eye began to fail, and at the end of four months vision equaled light perception. About a year later the vision of the left eye began to fail, and at the same time that of the right eye began to improve; eight months later, that of the left eye also began to improve. At the time of examination in each eye, only the anterior capsule was present. It was wrinkled and presented a buttonhole-like opening. In the left eye, some cortical matter remained. With plus 11 diopter spherical lenses vision equaled 20/30, and with plus 15 diopter lenses, Jaeger's test type could be read. The absorption of the lens was attributed by the patient's family to the constant local use of eggs, honey and olive oil. The patient had nephritis.

W. ZENTMAYER.

Vitreous

OBSERVATIONS ON THE CLINICAL VALUE OF THE OPERATIVE TREATMENT OF OPACITIES OF THE VITREOUS. W. WEGNER, Klin. Monatsbl. f. Augenh. **82**: 453 (April) 1929.

Failures of nonoperative treatments expected to clear up opacities of the vitreous prompted Elschnig to remove, by suction, a portion of the diseased vitreous and to replace it by physiologic solution of sodium chloride. His suggestions were not favored. Zur Nedden removed the vitreous by suction without replacing it. The results were fairly satisfactory, but complications endangered this procedure. Bliedung, therefore, resorted to a posterior sclerotomy, omitting suction by means of a cannula.

Wegner reports his results, with eighteen patients, of twenty-two posterior sclerotomies and thirteen removals of the vitreous by suction. The opacities were the result of injuries to the eyes in four patients, of spontaneous hemorrhages in

three cases, of uveitis in ten, and of postoperative infection in one case. Only one of the four cases of injuries was successful: the sclerotomy produced cessation of the intra-ocular infection and resulted in clearing the vitreous. The other three cases of this group were free from infection. The author, therefore, doubts whether vitreous of normal structure can be cleared at all by the operative procedure. He considers it safer to wait until pathologic changes, for instances liquefaction, have developed.

One of the spontaneous hemorrhages in the vitreous was remarkably improved. Here the diagnosis which, on account of the density of the opacities, had been impossible before could be made after the operation. Another case remained unchanged, one grew worse. In the second case the suction was technically impossible, while the sclerotomy allowed sufficient vitreous to escape. In a case of uveitis three sclerotomies were done with good results. In another some result was obtained by the sclerotomy after an unsuccessful attempt of suction had caused a decided deterioration of the vision. With the exception of two all other cases of this group were failures. One, a case of chronic tubercular choroiditis, was improved by the sclerotomy from 5/30 to 5/10. The other, a case of myopia of 12 diopters, yielded some improvement by the sclerotomy; beginning detachment of the retina remained unchanged. This experience supports the statement of Bliedung who claims that the danger of detachment of the retina after posterior sclerotomy is small.

The last case, that of postoperative infection, brought to light the remarkable feature that one posterior sclerotomy was sufficient in reducing the glaucomatous pressure to normal tension, and to stop the infection at the same time. Wegner, therefore, recommends this operation in this class of cases. Posterior sclerotomy, in the author's opinion, excludes the trauma and the enormous change of the intra-ocular tension brought on by the removal of vitreous through suction. After a sclerotomy, on the other hand, not more vitreous will escape than necessary to normalize the tension of the sclera. Insults to the intra-ocular vessels can be reduced to a minimum by just allowing the vitreous to escape slowly. Intra-ocular hemorrhages are rare. The removal by suction, again, is often technically impossible while mostly vitreous can be freed by means of the sclerotomy; it is, finally, simpler, technically, than suction. Both processes result in stimulation of the intra-ocular blood circulation and a greater afflux of bactericidal substances. Both may be repeated; none of them is entirely free from untoward incidents. It is advisable, therefore, to use them only in those cases which cannot be improved by the resorptive treatment, and in eyes which have already suffered a reduction of the vision to such an extent that nothing can be lost. The posterior sclerotomy is the superior procedure.

K. L. STOLL.

Glaucoma

THE VASCULAR STATE AND GLAUCOMA. F. P. CALHOUN, Am. J. Ophth. **12**:265 (April) 1929.

The author made a study, similar to Charlin's, of sixty-four patients to determine the cardiovascular state in simple glaucoma. Three of these patients were in the third decade, seven in the fourth, eighteen in the fifth, twenty-five in the sixth and twelve in the seventh. A hereditary tendency was noted in ten cases and was doubtful in six others. The observations were: (1) vascular disease in 95 per cent (Charlin, 90 per cent); (2) syphilis in 15 per cent of the vascular group, and in 14 per cent of all cases (Charlin, 57 per cent); (3) nephritis in 40 per cent of the vascular cases, and in 37 per cent of all cases; (4) abnormally

high systolic pressure in 42 per cent (Charlin, 62 per cent); (5) abnormally high diastolic pressure in 57 per cent, and (6) dilatation of the heart or aorta in 60 per cent (Charlin, 59 per cent). The author concludes that cardiorenal disease is closely allied with glaucoma, and suggests that it may even be an etiologic factor in the latter.

W. S. REESE.

ON GLAUCOMATOUS CUPPING WITHOUT RISE OF INTRA-OCULAR PRESSURE. K. VOM HOFE, Ztschr. f. Augenh. **100-101**:414, 1929.

The author describes those cases of typical glaucomatous cupping of the disk in which no increase in intra-ocular pressure above normal occurs. These were first described by Schnabel under the heading "cavernous atrophy of the optic nerve" and recently by Elschnig as "Degeneratio Nervi optici."

He maintains that no case should be included in this category unless the tension remains within normal limits throughout the day and night, and after the use of provocative drugs (homatropine).

Four cases are reported. He believes that the cupping may not necessarily be due to the penetration of pathologic fluid into the optic nerve in the manner described by Schnabel and Elschnig, but may also arise as the result of focal degenerations in the nerve due to arteriosclerosis.

FRANCIS HEED ADLER.

Retina; Optic Nerve

THE RETINAL ARTERIAL TENSION IN CEPHALORACHIDIAN HYPERTENSION. P. BAILLIART, Ann. d'ocul. **166**:271 (April) 1929.

The object of this paper is to determine the state of retinal tension in cranial hypertension. The most important ophthalmoscopic sign in the latter condition is papillary stasis, but choked disk exists in certain forms of general arterial hypertension, in some diseases of the orbit, of the nerve and of the globe itself. Therefore, one should not depend alone on choked disk for a diagnosis of intracranial pressure.

Papillary stasis is not always present in intracranial hypertension. However, especially in tumors of the brain, one finds the highest percentage of stasis, but even these may cause an intracranial hypertension without showing choked disk. The normal retinal arterial tension with the tonoscope is: diastolic, 30 to 35, and systolic, 75 to 80. The retinal tension is to the humoral as 54 is to 100 for the systolic and as 75 is to 100 for the diastolic. Every time the retinal diastolic pressure is more than half the diastolic humoral pressure, one may say that there is relative retinal arterial hypertension. This sign may indicate intracranial hypertension.

Claude, Lamacle and Dubar examined twenty-six patients with intracranial hypertension and without papillary stasis. They found increased diastolic retinal pressure in twenty-four cases. In the two that did not show this condition, a carotid sympathectomy of both sides had been performed several months before. They concluded that diastolic retinal hypertension is an advanced sign of intracranial hypertension. The elevation of the former precedes the appearance of choked disk and thus permits an early diagnosis.

Experimentation and clinical experience have shown that alteration of rachidian tension causes a corresponding change in the retinal diastolic pressure. Is the change in the two tensions equal? No. The reactions are proportional neither in intensity nor in effect.

If a lumbar puncture is made, causing a drop in the cerebrospinal pressure, what becomes of the retinal pressure? In a patient observed during one-half hour, the latter mounted as the former receded. Other workers, on the other hand, found a fall of retinal pressure. It is not simply a question of passive pressure, but one of vasomotor reaction, varying with each patient.

Why does not the retinal arterial pressure translate the state of the spinal pressure? Because hypertension of the spinal fluid is not constant. Evolution of this tension shows it to exaggerate, diminish, disappear and reappear. It has not the fixed character of the retinal tension.

What is the state of the retinal pressure in a case of intracranial hypertension manifested by papillary stasis? Thus far, it has been determined that in choked disk hypertension is inconstant, and that an established hypertension disappears when stasis arrives.

Some practical conclusions by the author are: If a patient presents a well defined choked disk, he probably has intracranial hypertension, but with certain reservations, already noted. If, however, the disk shows only a slight or no indistinctness of its edges, then the tonoscope is of value in determining cerebral hypertension. If the diastolic retinal arterial pressure is higher than half the diastolic humoral tension, there is increased retinal arterial pressure, a sign that indicates increased intracranial pressure, providing: (1) the disaccord between the two pressures is distinct, the retinal pressure being superior by a centimeter to the half of the humoral, (2) there is no optic atrophy and (3) there is no general arterial hypertension.

Some writers think that the position of the head affects the retinal tension. The author thinks that it makes no difference, though he prefers the sitting position.

Determination of the difference of the retinal pressure between the two sides may show not only which side contains the tumor, but also the lobe.

HUNTER W. SCARLETT.

A HAEMANGIOMA OF THE MENINGES INVOLVING THE VISUAL CORTEX. R. F. MOORE, Brit. J. Ophth. **13**:5 (May) 1929.

A boy, aged 12 years, complained only of defective vision of his left eye. Three years before, vision in this eye was 6/12. It had grown worse in the past year. A nevus of the left half of the face involved the eyelids. At the time of presentation, vision in the right eye equaled 6/9, partly, and that of the left 6/6, partly. There was an incomplete right homonymous hemianopia, a slight congenital dislocation of the lenses and a small coloboma of the left optic disk. A diagnosis of nevus of the visual cortex was made. This was confirmed by the roentgenogram which showed a tumor composed of a new growth of large vessels. A lateral roentgenogram showed the growth to be acutely wedge-shaped, the apex being far forward in the temporal region and apparently being situated superficially under the bone in this region. The base of the wedge was at the occipital pole immediately above the tentorium and was therefore closely related to the visual cortex. The dense shadow was probably due to calcification of the vessel walls. Mention is made of a number of reported cases of this kind. Buphthalmos is often associated, as is also heterochromia iridis. Lesser anomalies, such as occurred in the present case, are encountered. The ocular abnormality, when unilateral, in all instances was on the same side as the tumor of the brain. The author advises that in all cases of buphthalmos a roentgenogram of the skull be taken. He repeats a suggestion made by him several years ago that in cases of melanoma of the choroid one should watch for intracranial tumor. W. ZENTMAYER.

Ocular Muscles

PARALYSIS OF THE OCULOMOTOR NERVE IN FRACTURES OF THE BASE OF THE SKULL. J. S. CHARAMIS, Arch. d'opht. **45**:759 (Dec.) 1928.

After a brief historical introduction, the author describes the anatomic relations of the arachnoidal portion of the third nerve in cases that he has observed. The relations of the nerve to the vessels and especially to the bony structures are emphasized. He next discusses the pathology. He thinks that the course of the nerve in the middle fossa is a most important factor, in view of its close relation to the posterior clinoid processes and its path through the dura.

From a clinical standpoint, paralysis of this nerve has in itself no absolute value in regard to prognosis. If it is immediate and accompanied by gross signs of increased intracranial pressure, the outcome will probably be fatal. If the intracranial pressure is moderate, consciousness will return.

As a general rule, a complete paralysis will not be permanent and a patient with partial paralysis will tend to recover. A bad prognosis should not be hurriedly made, for the condition may be merely caused by compression.

The author concludes by pointing out the importance of further study of these patients after recovery. Other neurologic evidence may lead to a definite localization.

S. B. MARLOW.

CONGENITAL PTOSIS AND MUSCULAR ANOMALIES OF THE EYE. AMADEO NATALE, Arch. de oftal. de Buenos Aires **4**:14 (Jan.) 1929.

The author reports the case of an Argentine, aged 26, who, since birth, had presented a faulty position of his eyes. There were no personal or hereditary antecedents, eight brothers having normal eyes.

The patient presented a slight inclination of the head toward the left, the rotatory movements of the head being normal. There was a moderate ptosis of the right upper lid and a wrinkling of the forehead showing action of the occipitofrontalis, by means of which he partially corrected the defect. Both eyes were strongly deviated toward the right with no vertical displacement. On looking toward the right, the right limbus reached the commissure, with a 4 to 5 mm. displacement; the left limbus showing only a 2 mm. displacement. On looking toward the left, an inward displacement of 4 to 5 mm. was observed in the right eye, and an outward displacement of 2 mm. in the left. On looking upward, the patient strongly contracted the right occipitofrontalis, obtaining an 8 mm. opening of the right palpebral fissure, the left opening normally; the right eye remained immovable, while the left moved readily with some fixation by the internal rectus. On looking downward, the right eye continued immovable, while the left eye moved well, with fixation by the internal rectus. The right pupil was round, with a 4 to 5 mm. diameter, showing a slight reaction to light; the left pupil was round with a diameter of 7 mm. and a good light reaction; reaction to accommodation was almost absent on the right side and was normal on the left. Vision in the right eye was 3/10; in the left eye it was normal. The fundi were normal. There was no diplopia, nystagmus or vertigo. There was no disturbance in the gait, and no functional disturbance of the trigeminus. The ears were normal. The general condition was good. Under these circumstances, the author decided to operate, with the purpose of correcting the forced displacement of both eyes toward the right and the faulty position of the head.

The operation revealed a most interesting set of muscular anomalies:

A tenotomy of the left internus showed a powerful tendon inserted at barely 2 mm. from the corneal margin. The tenotomy obtained only a 2 mm. displace-

ment of the eyeball. An advancement of the left externus revealed a replacement of this muscle by tendinous bundles, inserted at from 8 to 9 mm. from the limbus, the belly of the muscle being poorly developed. Although some further displacement of the left eye outward was obtained, the result was insufficient. A tenotomy of the right externus revealed a double insertion at 8 mm. from the limbus, the two tendons running parallelly backward for some distance and later converging. The insertion of the right internus was situated at 8 mm. from the corneal margin, and the muscular belly was partially replaced by tendinous bundles.

With these operations an approximate correction was obtained in the deviation of the eyes to the right, the rotation of the head disappearing, both eyes and head being directed straight forward.

In a subsequent operation, a complete absence of the right superior and inferior recti was demonstrated.

The author refers to a prior paper, in which he reports several cases of defects or absence of the external recti and reviews the literature on ocular anomalies up to that date.

Since the former publication, Adrogué has reported a similar cases. Krayse, Ledouble and Lawford have noted an absence of the internal recti, Seiler and Steinheim of the superior rectus, Stieren and W. E. Davis of both inferior recti, Posey of one inferior rectus, Coover of the superior and inferior recti, Hartes and Seiler of the obliqui and finally Klincosh found a case of total absence of all the ocular muscles.

Posey, in a strabismus operation, found an insertion of the external rectus on the eyeball by means of two symmetrical tendons, 4 mm. broad; both were continued into separate muscular bellies, parallel to each other, which were lost in the bottom of the orbit.

In the author's case, the right external rectus was inserted by means of two tendons, the upper one 2 mm. above the horizontal meridian was 5 mm. broad, the lower one 3 mm. below the horizontal meridian was 4 mm. broad. Both ran parallel for some distance, then toward the orbital apex they converged, probably fusing into a single mass.

Riewicz quotes a similar case of an internal rectus inserted into the eyeball by two tendons, separated vertically by a distance of 4 mm., a dissection showing a decrease of the separation, with the formation of a triangular space, the apex of which was situated at 16 mm. from the corneal margin.

Macalister has also observed an internal rectus with a double scleral insertion. Dieffenbach and Behr have also reported a bifurcation of the muscle, Zogorky and Albinus have found double external recti.

Whitnall found a fleshy bundle 7 mm. long by 2 mm. broad, which passed from the external rectus across the posterior third of the orbit, under the optic nerve and joined the central fleshy portion of the inferior rectus.

Fuchs, Diffenbach and Pfluger have noted great deviations from the normal in the position of the scleral insertions of the ocular tendons, up to a 2.5 mm. difference, which the author has been able to corroborate in connection with the left internal rectus and right external and internal recti.

These anomalies have been attributed to disturbances in the intra-uterine development of the common embryonic premuscular mesoblast.

Many cases of squint depend on these anomalies, and it is only by a correct appreciation of the fact and a better knowledge of the different peculiarities that the surgeon can, in certain instances, overcome the difficulties present and restore the parallelism of the ocular axes.

Whitnall, from numerous dissections of the orbrit, recognizes that these anomalies are much more frequent than one would infer from a study of the literature on the subject, not being noticed *intra vitam* on account of the compensatory action of the other muscles.

According to Fuchs, the normal compensatory equilibrium can be disturbed by irregularity in the relations between the positions of the different muscular insertions.

The case presented by the author differs from the others hitherto reported in the forced deviation of both eyes to the right, in an accompanying right-sided ptosis, in the slight compensatory rotation of the head toward the left, in the fixation of the eye in this forced position, toward the right, and in the operative proof of abnormal insertions of the recti and has in common with other reported cases a bifurcation or double insertion of the right external rectus.

In view of the congenital character of the lesions, of the absence of any cranial lesion, as well as of any sign of any focal cerebral lesion, the author considers that in this case, apart from the muscular anomalies noted, there also existed some disturbance of the innervation equilibrium of the ocular muscles of a reflex nature.

FINLAY.

PALSIES OF THE THIRD NERVE WITH CYCLIC ALTERNATION OF SPASM AND RELAXATION IN THE PARALYZED MUSCLES. A. BIELSCHOWSKY, Arch. f. Ophth. **121**:657 (March) 1929.

In the literature, twenty-eight cases of palsies of the third nerve have been described which show the striking phenomenon of cyclic alternation of spasm and relaxation in the parlyzed muscles. Bielschowsky found 5 such cases among the 1,700 cases of palsies of the eye muscles. In these cases the palsy of the third nerve was either present at birth or showed up during the first two years of life. Several cases showed just the paralysis for a few years, and later the cyclic phenomena. Bielschowsky's first case was in a boy, aged 13 years, who had been operated on by Uhthoff seven years before Bielschowsky saw him. Uhthoff performed an operation for ptosis and tenotomy of the externus combined with advancement of the internus rectus muscle on the right eye. At that time, no cyclic movements of the eyeball were found. Bielschowsky found the left eye of the patient normal except for rotatory nystagmus. The right eye showed almost complete ptosis; the strongest impulse caused an elevation of the upper lid so that the lower half of the cornea could be seen. The right eyeball stayed in a middle position. No adduction, elevation or abduction was possible. There was reduced ability to depress the eyeball (isolated action of the superior oblique). The right pupil, the right upper lid and the right accommodation muscle showed the cyclic phenomena as follows: In the stage of perfect relaxation, the left normal pupil was 6 mm., and the right 7.75 mm. wide and the right upper lid hung down, entirely "paralyzed." After about one minute slight and transient contractions started out in the right upper lid and in the right pupil (hippus). Gradually these contractions became more frequent and more marked until at the end of the third minute the pupil contracted to a width of 2 mm. and the upper lid was elevated to such an extent that the lower two thirds of the cornea could be seen. The pupil and the upper lid remained in this condition for from ten to twenty seconds without showing any movements. After that the pupil dilated to a width of 8 mm., and the upper lid dropped down to perfect relaxation without showing any spasmodic interruptions of the relaxation. The relaxation took place within about forty seconds. The ciliary muscle took part in this cyclic phenomenon by changing the

refraction of the eyeball (found by sciascopy) by 8 to 10 diopters. The frequency of the cycle depends on the psychic disposition of the child. Intended voluntary eye movements had a typical influence on the cyclic phenomena. If the patient was asked to fix an object in the right half of his field of motion, then his right eye, although it did not move because of the palsy of the externus muscle, was under the influence of an impulse which increased the tonicity of the right internus rectus muscle. Under these conditions, the spastic phase of the cycle was marked and considerably retarded. The opposite phenomenon took place if the patient fixed an object in the left half of his field of vision.

About the same observations were made in all of the twenty-eight cases reported to date. Therefore, it seemed justified to separate these cases of palsies of the third nerve from all the other cases in which cyclic phenomena could not be observed. It could be expected that this special group of cases had its own etiology and localization. Some of the symptoms which they showed were pointing toward a lesion of the trunk of the third nerve, but the principal mechanism was that the impulses which were coming from the cortex did not have any influence on the nuclei of the third nerve. Therefore, Bielschowsky believed in a supranuclear localization of the lesion in these cases. In order to explain the fact that impulses for voluntary movements modified the course of the cyclic movements, Bielschowsky assumed changes of the circulation in the region of the nuclei. He thought that the impulse for the rotation of both eyes to the left caused a hyperemia in the left sixth and in the right rectus internus nucleus. This hyperemia changed the tonicity and the sensitiveness of the cells of the nucleus, and so the cyclic movements were modified. From the fact that only certain muscles showed the cyclic movements, Bielschowsy concluded that certain parts of the nucleus were damaged too, so that for the explanation of all the symptoms a combined nuclear and supranuclear lesion was to be postulated. It is striking that in most of these cases the movements of the other eye were normal, although one would expect that a severe nuclear lesion on one side would lead to some defects in the third nerve of the other side. At the present time it is still thought that the third nerve gets most of its fibers from the homolateral and some from the contralateral side. This theory does not apply to this special group of cases with cyclic motor phenomena. Therefore, further studies of the anatomy of the roots of the third nerve are necessary.

KRONFELD.

Orbit, Eyeball and Accessory Sinuses

PULSATING EXOPHTHALMOS. DEWAYNE HALLETT, Am. J. Ophth. **13**:710 (Sept.) 1928.

The condition was seen in a woman following a lacerated wound and severe contusion above the left eye. A bruit developed after twelve days. A diagnosis of pulsating exophthalmos was made after sixty-three days. For twenty-one days the treatment was physical rest. At the end of ninety days ligation of the common carotid was immediately followed by complete transient hemiplegia. The bruit returned on the one hundred and fourth day. The superior ophthalmic vein was ligated on the one hundred and thirty-third day. The bruit again ceased but proptosis and chemosis were greatly increased, and a neuritis with partial atrophy in the opposite arm and foot developed. At the end of one year the proptosis is absent, the optic nerve atrophic and the distant symptoms improved.

W. ZENTMAYER.

ORBITAL INVOLVEMENT FROM NASAL SINUS DISEASE SIMULATING CAVERNOUS SINUS THROMBOSIS. H. M. LANGDON, Am. J. Ophth. **13**:719 (Sept.) 1928.

The patient, a woman, aged 39, following an attack of grip with profuse mucopurulent nasal discharge complained of pain in the right side of the head involving the distribution of the upper and middle branches of the right trifacial nerve. The following day there was a third nerve palsy and some exophthalmos. The right ethmoid and antrum were found to be infected. All symptoms subsided following intranasal treatment. The author says that for twenty-four hours the chances seemed about evenly divided as to whether or not the condition was the early stage of a cavernous thrombosis. The only definite sign not present was edema over the mastoid which is not always present early. W. ZENTMAYER.

INTRA-OCULAR CYSTICERCUS: SECONDARY MIGRATION INTO THE ANTERIOR CHAMBER. BARSAN, Arch. d'opht. **45**:694 (Nov.) 1928.

The author first briefly reviews the literature and points out the rise in the incidence of this condition during the World War when the inspection of meat was not so rigid. He then reports in detail a case in which the cysticercus migrated into the anterior chamber. In September, 1926, a girl came under treatment on account of a severe iridocyclitis of the left eye for which no cause could be found. This condition cleared up under the usual treatment, and the eye remained quiet for a month, when on December 1 she noticed a sudden, momentary complete loss of vision of the same eye following which she observed a foreign body in it. Examination, especially after slit-lamp study, resulted in the diagnosis of a cysticercus in the anterior chamber. After a somewhat difficult removal, the diagnosis was confirmed microscopically.

The author thinks that the organism first became lodged in the ciliary body through the long posterior ciliary arteries and produced the iridocyclitis.

After a month of quiet, it penetrated into the posterior chamber from which it was carried through the pupil into the anterior chamber. Its passage through the pupil resulted in the momentary loss of vision. This unique course of events makes the case interesting. The outcome was satisfactory. S. B. MARLOW.

CONTRIBUTION TO THE PATHOLOGY OF THE DISEASES OF THE ORBIT. H. MAGNUS, Arch. f. Ophth. **122**:101 (May) 1929.

The author reports twenty-six cases of diseases of the orbit which were studied clinically and anatomically. Twenty-two of these cases had tumors; four cases belong to the group of cellulitis orbitalis. Three of these showed anatomically the picture of thrombophlebitis with infected thrombi in the orbital veins. The next stage was a hemorrhage in the surrounding tissue, then the wall of the vein was grossly perforated and an abscess developed around the perforated vein. This was the mechanism in most of the cases of cellulitis orbitalis. Only in one case the author found diffuse infiltration of the orbit ("streets of leukocytes") without special involvement of the orbital veins. This type, however, later on leads to thrombophlebitis too.

Among the tumors were four cases of round cell sarcoma and five cases of spindle cell sarcoma. Two of these started as sarcomas of the choroid. The patients did not present themselves until the retrobulbar growth of the tumors caused exophthalmos. The intra-ocular development of the tumor had not caused any subjective symptoms. Anatomically in both cases the same picture was found: Phthisis bulbi with complete destruction of retina and optic nerve, the orbital tumor surrounded and compressed the phthisic eyeball.

In one case a small flat sarcoma of the choroid was found which had perforated the sclera and led to a large orbital tumor. The intra-ocular tumor could not be diagnosed *intra vitam* because of its flat growth in the choroid without injuring the pigment epithelium. All the cases of small intra-ocular and large orbital sarcomas must be considered as primary tumors of the choroid. It has not been proved that an orbital tumor can perforate the sclera from behind and lead to intra-ocular extensions.

In another case of spindle cell sarcoma which had started out in the region of the caruncle, the marginal parts of the tumor showed connective tissue with marked proliferation of lymphoid tissue (lymph follicles). The case was considered as a sarcoma which caused the development of an inflammatory pseudotumor by toxic irritation of the surrounding tissue. So lymphatic tissue can be found in the orbit, although the normal orbit does not contain any lymphatic tissue.

One case of lymphomatosis of the orbit (especially within the rectus superior muscle) was thought to be of traumatic origin because no other etiology could be found.

Three cases of metastatic carcinomas of the orbit were observed. The first site in the orbit is usually in the eye muscles, so that diplopia is the typical symptom of a metastatic carcinoma of the orbit (primary tumor in the breast or in the stomach). In one case the metastatic tumors were first located in the uvea of both eyes and extended from there along the ciliary nerves in the orbital tissue. In the cases of metastatic carcinomas of the uvea the left eye is usually affected first because the left carotid artery is a direct branch of the aorta, while the right carotid artery comes from the arteria anonyma, subtending a blunt angle with the latter, so that cells are more easily spread through the left carotid artery.

KRONFELD.

General Disease

DENGUE FEVER AND ITS OCULAR COMPLICATIONS. GABRIELIDES, Ann. d'ocul. **166**:183 (March) 1929.

Dengue fever belongs to the exanthematous diseases and is caused by a microbe, which is not yet known, but is transmitted from one person to another by an intermediary host, the mosquito.

It has actually been proved by inoculations that the microbe of dengue fever circulates in the blood and belongs to the group of filtrable microbes.

The symptoms are divided into two general groups, those appearing during the evolution of the disease and those manifesting themselves after recovery and during convalescence.

In the first group are included: (1) conjunctivitis, mostly a congestion of the membrane with a little secretion; (2) blepharitis, with redness and edema of the lids, and (3) muscular pains of the lids and of the ocular muscles coming on when the eyes are closed or when the globes are moved about.

The symptoms belonging to the second group are as follows: (1) diplopia from muscular atony, paresis or paralysis; (2) photophobia, muscae volitantes, scintillating scotoma, etc.; (3) keratitis; (4) iritis; (5) metastatic ophthalmia, and other intra-ocular infections caused by localization of the germ of dengue fever or its toxin in the tissues of the eye or optic nerve; (6) glaucoma; (7) recurrent retinal hemorrhage; (8) optic neuritis.

The diagnosis may be made comparatively easily during an epidemic, by judging the general symptoms of the disease, but in a sporadic case it is much more difficult.

Examination of the blood shows the red cells to be normal, with a fairly well pronounced leukopenia. The blood picture becomes normal quickly, so that it cannot well be used for diagnosis.

Treatment is symptomatic. Little importance is attached to the instillations or injections of serum obtained from patients cured of the disease.

Prophylaxis consists of lavage of the eyes with a bland collyrium.

H. W. SCARLETT.

Tumors

ANATOMIC RESEARCH INTO THE CAUSES OF OCULAR HYPERTENSION IN TUMORS OF THE CHOROID. KOLIOPOULOS, Ann. d'ocul. **166**:206 (March) 1929.

How should one explain the hypertension which so often appears during the evolution of choroidal tumors? The views of several authors were given, and the concensus was that the hypertension was due to three factors: the modifications in the iridocorneal angle, the dimensions of the tumor and the intraretinal exudate.

Of thirty-three cases studied, the histologic observations were given in twelve. Five of these presented no rise in intra-ocular tension, while seven others showed an increase in pressure. When the results in these cases are compared with the clinical observations, it is interesting to note that the condition of the iridocorneal angle, the size of the tumor or the retinal exudate did not furnish certain information relative to the ocular hypertension.

Uveal sarcoma may develop in the posterior part of the globe, the most frequent location being at the equator or at the ciliary region and the iris.

The site of the sarcoma affects the ocular tension. In a general manner, hypertension appears more frequently when the tumor is situated in the anterior part of the globe (equator, ciliary region) than when it is located in the posterior part.

The only real conclusion that was obtained from this investigation was that a tumor, especially a sarcoma situated in the anterior segment of the uvea, caused an increase of tension more rapidly than did those in the posterior segment.

H. W. SCARLETT.

PRIMARY EPITHELIOMA OF THE MEIBOMIAN GLAND, INVADING THE ORBIT WITH ATROPHY OF THE GLOBE: REPORT OF A CASE. Y. SHOSI, Arch. d'opht. **46**: 145 (March) 1929.

In 1922, Giovanni found reports of forty cases of malignant tumors of the meibomain gland in the literature, twenty-four of the growths being adenomas and sixteen epitheliomas. DeLapersonne added a report of a case of epithelioma in 1923. The author presents in abstract eight additional cases which have appeared in the Japanese literature and which have not been generally available. To these he adds a ninth personal observation. All the tumors were epitheliomas. They appeared without any known or accidental cause. They developed most commonly after the age of 40, although one occurred at 35. In six of nine cases, the upper lid was primarily affected. The tumor grows slowly, requiring from three to five years to involve the whole lid. Its size depends on its growth. Microscopically, it was found to have started from round or ellipsoid cells with large nuclei in eight cases. In one, it appeared to have developed from pavement epithelium. From the standpoint of recurrence, it is malignant. When the orbit is invaded, the eye is destroyed and life endangered.

S. B. MARLOW.

NOTE ON GLIOMA. MONTALTI, Ann. di ottal. e clin. ocul. **57**:268 (March) 1929.

A case is briefly reported in which roentgen treatment was given for early glioma retinae in involvement of an eye following enucleation of the other eye. After three series of treatments in two months the tumor was apparently arrested and even became somewhat smaller than at first. This condition has been maintained for two years. The vision is not stated.

S. GIFFORD.

TUMORS OF THE OPTIC NERVE SHEATHS. PAULINA SATANOWXY and ESTEBAN ADROGUÉ, Arch. de oftal. de Buenos Aires **4**:142 (March) 1929.

The authors briefly review recent studies on the pathologic anatomy of tumors of the optic nerve, according to which the optic nerve and its sheaths are considered as a prolongation of the cerebrum and its meninges, leading to the interesting work of Oberling and Nordmann (1927), which tends to establish a relationship between meningocerebral tumors and those of the optic nerve, especially between meningeal tumors and those of the optic nerve sheaths. These investigators seek the origin of these tumors in the arachnoid cells, which they, differing from Cushing, locate in the pia and consider of a special nature distinct from connective tissue and endothelial cells, calling them meningoblasts and the tumors to which they give rise meningoblastomas.

The fact that the cells lining the free pial surface have another aspect explains the different appearance of tumors according to their origin from one or another group of cells, which different authors have tried to compare with tumors from other parts of the body, with the production of great confusion in their classification. In order to be able to diagnose a meningoblastoma, it is necessary to examine the preparation slowly and with great care, as the typical elements are often to be found only in one or two places, making the diagnosis difficult. It is necessary to insist on the separation from the dura at the periphery of the tumor, where they originate, for "meningoblastomas are not heterogeneous tumors, but an evolutionary variety of one and the same cellular layer, the meningoblast." In epitheliomatous and pseudosarcomatous meningoblastomas, apart from the other elements, are to be found some fusiform cells disposed in bundles or in spirals with the production of small calcospheres which are to be found in the limits of the tumor with the dura. Other tumors to be found are the psammomas, the endotheliomas. The meningoblastomas are distinguishable from all other tumors of the optic nerve sheath by the sole presence of these calcospheres. Psammomas are typical endotheliomas, while meningoblastomas usually show a mixed cellular composition, with a predominance of small somewhat fusiform cells, some arranged in spirals, others irregularly with larger round cell nests. As the pia is of mixed ectodermic and mesodermic origin, and the dura solely of mesodermic origin, one is apt to find mixed tumors at this site.

These tumors usually develop in young subjects and present as their most prominent symptom a slowly developed exophthalmos, with reduction in sight, not always noticed by the patient. In a few cases their development is more rapid, and exceptionally there is a spontaneous reduction. This exophthalmos is directly forward and irreducible. In the course of its development the growth may be more pronounced on one side with lateral deviation of the eyeball. At first, the movements of the eyeball are not affected. As a rule there is little pain. A reduction in sight is one of the earliest symptoms; it may precede the exophthalmos. The fundus may at first be normal, even with total blindness, optic nerve atrophy appearing later. If the tumor is situated near the eyeball, papillary edema is found, with venous stasis and hemorrhages and white spots in the retina. Thrombosis of the central vein, extension of the tumor to the papilla with cystic formations

in this situation have been reported. The exophthalmos may give rise to corneal lesions, with a consequent destruction of the eyeball. Rarely cerebral symptoms are found.

The diagnosis is usually easy. The prognosis, as a rule, is bad for the eye, but the condition is not, as a rule, fatal.

The author next gives clinical and pathologic reports of six cases of primitive tumors of the optic nerve sheaths, illustrated with numerous photomicrographs.

FINLAY.

MELANOMA AND SMALL SARCOMAS. SCHAPPERT-KIMMSYER and HOWER, Arch. f. Augenh. **100-101**:21, 1929.

This is a review of cases reported previously in the literature as microscopic sarcomas. Small tumors in the choroid in an eye with a typical sarcoma of the iris are also described. These tumors showed anatomic and clinical similarities to melanoma, nevoid pigmentation and microscopic sarcoma. The authors consider the diagnosis of sarcoma in these cases of microscopic sarcomas insufficient — the type of cell is not indicative of sarcomas, and an infiltrative growth has not been proved. Many of these cases are more correctly classified as melanomas.

One may compare this enlarged classification of melanomas with the ordinary skin nevus. The diagnostic significance of the nevus cell is discussed; they may be absent in unquestioned pigmented skin tumors, and therefore their presence in the choroid is no conditio sine qua non for a diagnosis of nevus of the choroid. Many of the cells in choroidal melanomas are similar to the true nevus cell in the skin. There is an especial similarity between the so-called "blue nevus" of the skin and melanomas of the choroid.

The authors prefer the name melanophakos for conditions such as those described.

FRANCIS HEED ADLER.

Sympathetic Ophthalmia

OPTIC NEURITIS IN SECOND EYE FOLLOWING PERFORATING WOUND AND EXCISION. F. LAW, Brit. J. Ophth. **13**:364 (July) 1929.

The first case occurred in a man, aged 20 years, who had received a perforating wound of the right eye involving the cornea. The iris was adherent, but not prolapsed. The lens was grossly injured. Vision consisted of the ability to count fingers at 12 inches. The left eye was normal. The synechia was divided and the lens evacuated. Three weeks later, the synechia was again divided. Marked reaction was present. Three weeks later, tension was low. The differential white count was normal. The eye was excised sixteen days after the injury. Two months after the enucleation, vision in the left eye equaled 6/36. There was slight blurring and pallor of the papilla. Roentgen examinations of the skull gave negative results. The blind spot was not enlarged. There was a small central scotoma for green and red. Despite the usual treatment including injection of milk, six months later vision equaled counting fingers at 2 meters. The second case was seen in a girl, aged 16 years. In the left eye there was an incised wound of the cornea, with injury to the lens and prolapse of the iris. The eye was excised on the fifth day. The right eye was normal. About four and a half months later there was 3 diopters of swelling of the optic papilla. Vision equaled counting fingers at 1 meter. The field was full, and the blind spot showed slight horizontal enlargement. Seven months from the time of the injury, vision was 6/9. The author states that the possibility of the involvement of the second eye being a pure coincidence in both cases must be admitted.

W. ZENTMAYER.

Society Transactions

EDITED BY DR. GEORGE S. DERBY

COLLEGE OF PHYSICIANS OF PHILADELPHIA
SECTION ON OPHTHALMOLOGY

A. G. FEWELL, M.D., *Secretary*

March 21, 1929

C. E. G. SHANNON, M.D., *Chairman*

A CASE OF MASSIVE EXUDATIVE RETINITIS. DR. S. L. OLSHO.

A young woman, aged 19, presented massive exudative retinitis. The mother died of a tumor of the brain at the age of 36, and the father of a stroke at 74. One sister had bilateral retinitis pigmentosa. Two brothers and four sisters were healthy. The maternal grandfather and two aunts died of tuberculosis.

Physical examination showed that the patient was otherwise healthy. The Wassermann and Pirquet reactions were negative. The lesion of the left eye was first noticed one year ago.

CILIUM IN THE ANTERIOR CHAMBER FOR SEVENTEEN YEARS. DR. G. H. CROSS.

A young man, aged 26, had been referred because of a foreign body in the cornea of the left eye. On examination, a large cilium was discovered, one end of which apparently was fastened to the posterior surface of the iris at about 3 o'clock. The free end projected forward and nasally across the pupillary space.

On questioning, the patient recalled that seventeen years ago he had been struck in the left eye with a heavy piece of steel spring. There was a scar on the cornea showing the probable wound of entrance of the cilium that was now in the anterior chamber. There was no apparent cyst formation, and the patient had no discomfort. The removal of the cilium was not contemplated, as the patient said he had no trouble and was satisfied to let well enough alone.

INVESTIGATIONS ON THE CRYSTALLINE LENS. DR. A. C. WOOD, Baltimore.

Dr. Wood read a paper telling of the work of various investigators along this line, and pointing out that the physician is still a long way from the solution of many problems involving the crystalline lens.

DISCUSSION

DR. FRANCIS HEED ADLER: The experimental attack on the problem of cataract reminds one of the fight with that mythical creature of the dim past who grew two parts immediately where one was cut off. As Dr. Woods has stated, the problem has been attacked from many angles; those attacks which were founded on earnest endeavor, rather than on superficial "hunches," have rewarded us richly. At the same time, one is confused by the vast amount of data that has accumulated and that keeps piling up with ever increasing tempo. The chemist has left us with a more complete knowledge of the chemical units of which the normal lens is made, but an analysis of the relation of these units to one another in cataract has not yet

been completed. The more the problem is studied the more complex does it become, as exemplified by the fact that now Dr. Woods is forced to speak of a gamma crystalline in addition to the alpha and beta forms previously recognized. With the artificial production of cataract in animals by irradiation with ultraviolet light, by deficient dieting and by extirpation of the parathyroid glands, knowledge is gradually closing in on the etiology of cataract; but the exciting factor or factors common to these conditions have not been decided on. The discovery by Gowland Hopkins of glutathione and its application to the autoxidation system of the lens by Goldschmidt, Adams and others have added intricate problems. Finally, with the serologic attack which Dr. Woods is so ably carrying on, I confess that the tangle becomes almost too difficult and the approaches too specialized for the ophthalmologist to penetrate. There is, however, one factor that applies to all experimenal work and that is most consoling. The development of any subject seems to occur in two phases. First, more and more details are accumulated, with apparently an increasing perplexity on the part of the investigators. Finally, however, the data, like the parts of a jig-saw puzzle, begin to group themselves together into recognizable units, each group having a definite relation to the others. I look to Dr. Woods to be able some day to put these pieces together, and then the picture will be complete and simple.

DR. I. S. TASSMAN: Dr. Woods' own investigations of the crystalline lens resulted in several noteworthy contributions. Just recently, he described the isolation of a third crystallin, which he called the Gamma crystallin and which he found to be an albumin. Moerner in his original classification of the proteins of the lens spoke also of an albumin which he stated existed in small amount, and which he did not investigate any further. In an earlier work, Woods and Burkey described the separation of the various lens fractions and the preparation of serologically pure antigens at their iso-electric point. It was also of significance that they found the beta crystallin undergoing spontaneous precipitation on withdrawal of the alpha fraction, and seemed to support the view of earlier workers that senile cataract formation is at least accompanied by a disappearance or replacement of the soluble cysteine-containing elements of the lens. This was often demonstrated by an absence of the nitroprusside reaction in a cataractous lens, whereas it is always present in the normal lens. This reaction was said to be due to the presence of cysteine, an amino-acid element of the tissues which is autoxidizable. In its oxidized form, cystine, it does not yield the nitroprusside reaction. Heffter, in 1911, described this oxidation-reduction as a process which takes place in the tissues, and depends on the action of the H of the SH group present. Since cysteine contains the SH group, its labile H is liberated when it is oxidized to cystine, and the reverse takes place in its reduction to cysteine. But cysteine had not as yet been demonstrated in its free state in the tissues. It was not until 1921 that Hopkins discovered that cysteine exists in the tissues in combination with glutamic acid as a dipeptide, to which he gave the name of glutathione. This substance showed the same oxidation-reduction properties in the tissues as had been attributed to cysteine, and is responsible for the presence of the positive nitroprusside reaction. Now since the nitroprusside reaction is present in normal lens and absent in cataract lens, it can be assumed that glutathione is not present in the cataractous lens in its reduced form. The relationship of the possible oxidation-reduction of glutathione taking place in the lens normally will require further study. This process in the tissues of the body is being investigated at the present time, and attempts are even being made to measure it. In the future, the possible development of methods suitable for this purpose may favor a better understanding and contribute to our knowledge of this biochemical process.

A Third Hundred Successive Cataract Extractions in-the-Capsule After Preliminary Subluxation with the Capsule Forceps. Dr. Arnold Knapp, New York.

After defining the type of senile cataract which is suitable for this procedure, Dr. Knapp spoke of the technic in the use of the capsule forceps, and the methods which he usually follows, emphasizing the necessity of the preliminary subluxation of the cataract before extraction in the capsule.

An analysis of a third series of 100 successive intracapsular cataract extractions was then given, the type of cataract, the mode of delivery and the visual results obtained being described. The visual results were 20/30 or better in 74 of 100. Vitreous was lost in seven. These cases were fully described, and the resulting vision given. Iris occurred in eight cases, which were also fully described. Wound reopening with hyphemia occurred in ten cases. Expulsive hemorrhage occurred in two; one required enucleation. Detachment of the retina occurred after one year in one case and after a year and a half in a second case, the vision after the operations at first being normal. Prolapse of the iris occurred in one case. Glaucoma appeared in no case, unless it was a part of cyclitis. In two cases, glaucoma preceded cataract; after intracapsular extraction, tension remained normal.

DISCUSSION

Dr. Luther C. Peter: You may be interested in contrasting an opinion of Isaac Hayes of eighty-two years ago, which appeared in the American revised edition of Lawrence's "Treatise on Diseases of the Eye," published in 1847. I quote the following: "When the section of the cornea is finished, the great difficulty of the operation is past; the rest is easy. All that remains is to rupture the capsule of the lens. The lens might by forced out without previously opening the capsule, but the vitreous would probably be expelled with it."

All will agree that the real difficulity begins after the section is completed, in contrast with this opinion expressed eighty-two years ago; some may agree with Isaac Hayes that the vitreous is apt to follow an intracapsular extraction. However, vitreous loss need not be any more frequent after a correctly performed intracapsular extraction than after an operation with capsulotomy. In my paper, which is to follow, I shall discuss briefly certain steps that tend to prevent vitreous loss in either type of operation.

Although I am an exponent of the intracapsular method, I believe that operators may be divided into two groups; first, those who might advantageously practice a modern form of extraction with capsulotomy; second, those in whose hands an intracapsular operation is justified. In the first group might be included all beginners and older operators whose extractions during any single year are comparatively few. In the second group might be included any operator who has a good surgical hand, and who has the opportunity for constant practice. Aside from the question the type of operation which is best adapted to a specific case, the individual operator's choice can be determined by his surgical ability and experience.

If we eliminate the question of the surgical skill required for each method and compare the results of the two methods, there can be no reason for a difference in opinion as to the much greater value of intracapsular extraction. As pointed out by Dr. Knapp, vitreous loss, iris incarceration, vitreous opacities, after-cataract and secondary glaucoma are all reduced to a minimum. Recovery is more rapid and is uncomplicated, and a high degree of visual acuity is assured. Personally, I am disappointed when central vision of 6/6 is not obtainable in my work, and 6/5

and even 6/4 is more often obtained than less than 6/6. I am speaking of averages and not of individual cases.

On other occasions, I have raised a protest before this section against discission for after-cataract, which is so often made necessary by methods involving capsulotomy, especially when the somewhat antiquated cystotome is used for rupturing the capsule. In my experience, there is no intra-ocular operation which is attended by more danger than discission of an after-cataract. Obviously, this operation can be avoided by removal of part or all of the anterior capsule by toothed forceps. Even under these conditions, there is an annoying complication, to which Dr. Knapp has not referred, which makes its appearance one or two years after the extraction, and reduces vision, unless it is met by a discission. I refer to epithelial activity. This may develop if any part of the proliferating section of the capsule is left in the eye. All these complications are eliminated by intra-capsular methods.

Dr. Knapp is to be congratulated on the excellent results from the standpoint of complications. It is rather remarkable that he should have but one case of iris prolapse in a series of 100 cases. Loss of vitreous in 7 per cent is average even in operations with capsulotomy.

As to the method itself, one's individuality and experience are apt to bring about some variation in the technic. Dr. Knapp prefers to rupture the zonula by means of smooth forceps, and deliver the lens by the method which he described. In an uncomplicated case, I prefer to use smooth Kalt forceps to complete the extraction, a Smith expression hook being used but little and with the slightest pressure. In my experience, if the lens is slowly withdrawn, vitreous will not follow. On the other hand, undue pressure with the Smith hook may cause vitreous presentation. Only experience can be one's guide, and my technic differs from that of Dr. Knapp only as the result of the extraction of many lenses. Possibly his method works best in his hands.

The point for grasping the capsule is of much importance. If it is grasped near the lower border of the pupil, tumbling of the lens on delivery is ensured, and breaking of the zonula is easier than when the capsule is grasped at a higher position. Furthermore, if the capsule ruptures, as it occasionally does, the anterior capsule in the pupillary space is in the grasp of the forceps and is removed, and needling for an after-cataract will not be necessary. If the capsule is grasped above, as recommended by Verhoeff, a rupture of the capsule will be above the pupillary space, and a discission may be necessary.

The method is ideal, and should appeal to the younger men who hope to give their best to their patients as their experience increases.

FURTHER DISCUSSION

Dr. C. E. G. Shannon said that he had been privileged to see Dr. Knapp perform the intracapsular operation in twelve cases. He was impressed, first, with the thoroughness with which the eye was placed under control prior to operation; second, the delicacy and deliberation with which Dr. Knapp carried out the entire operation; third, the clear, black pupil that is shown following the delivery of the lens—a delight to every operator; and lastly, and of considerable import, the absence of any accident in all of the twelve cases. Dr. Shannon said that such results as had been shown by Dr. Knapp in his review of the "last 100 cases" certainly merited the profound interest of every ophthalmic surgeon.

Dr. G. Oram Ring asked Dr. Knapp whether as a routine he did a complete iridectomy in connection with this removal of the lens by subluxation with the capsule forceps.

Dr. Barraquer said that he elects to incise a small piece of iris midway between the pupillary and the ciliary border, and added that a recent communication from another operator suggested the propriety of omitting the iridectomy altogether.

Dr. Ring noted that Dr. Knapp had had two choroidal hemorrhages in this last list of 100 cases and was interested to know how many accidents of this type Dr. Knapp had had in this entire intracapsular series of 300 cases. Dr. Ring's own experience in that particular type of tragic accident, in a series of 2,500 extracapsular cases, had been only one choroidal hemorrhage in each 500 extractions, and he was under the impression that Dr. de Schweinitz' experience had been similar.

Dr. Leighton F. Appleman stated that during the winter just past he had had ten cases of cataract in which the lens had been extracted in its capsule. In three, he had used the loop, carefully breaking the capsule at its upper border and gently insinuating the loop beneath the lens, and had delivered it without loss of vitreous. In the others, delivery was effected by pressure below with the Smith hook, but difficulty was experienced in breaking the capsular attachments below; in fact there was slight loss of vitreous in some, which, however, did not interfere with prompt healing.

The method described by Dr. Knapp appeared to him to be an ideal method of operating.

Dr. Arnold Knapp: I agree with Dr. Peter that discission in many cases is difficult, and the proliferation which takes place from the margins of the cut capsular wound frequently interferes with the final vision. This same proliferation has occurred occasionally in the anterior layers of the vitreous in the intracapsular cases.

In answer to Dr. Ring, an iridectomy is always done at the time of operation. I doubt whether the choroidal hemorrhage can be ascribed to the operation. When expulsive hemorrhage takes place, the presence of the suspensory ligament and posterior capsule would not prevent its occurrence.

In answer to Dr. Holloway, I am of the opinion that detachment of the retina, which occurred in two of these cases, cannot be ascribed to the operation. Still it is difficult to convince the patient of this.

In conclusion, I do not wish to say that the capsule forceps is the only way to subluxate a cataractous lens. It is, I think, the simplest way, as we are all experienced in handling a pair of forceps. I am convinced that the tumbling method is essential to the safety of the operation, and I feel that this is a method by which the advantages of the intracapsular operation can be obtained without subjecting the patient to the difficulty and risks of the original Smith technic.

Important Phases of a Satisfactory Extraction of Senile Cataract.
Dr. Luther C. Peter.

Dr. Luther C. Peter said that a change in method is indicated in this most important of ophthalmic operations when results are not satisfactory, and when it can be shown that accidents may be avoided by a change in technic. The complications which one endeavors to avoid are loss of vitreous, iris prolapse, vitreous opacities, after-cataract, secondary glaucoma and the necessity for more than one operation on a single eye.

Phases of lens extraction which tend to reduce these complications, in the author's experience, are:

1. Efficient anesthesia and motor block. Deep anesthesia of the ciliary ganglion is practiced, in addition to the usual local anesthesia, as well as motor block, both of which are practiced in all cases if the blood sugar is normal.

2. Marginal lid sutures. They are introduced to control the lids during operation, and are tied after the extraction. They are left in place four or five days.

3. Lids held by a well trained assistant. A blepharostat is never used because of difficulty in closing the lids promptly when required.

4. A generous conjunctival flap.

5. Two conjunctival sutures to prevent iris prolapse and ensure rapid closure of the wound. A single suture favors iris prolapse. These sutures are tied immediately after the lens is extracted, and toilet of the wound and irrigation of the anterior chamber, if necessary, are carried out with safety.

6. Intracapsular extraction by means of the Kalt forceps. A Smith expression hook is of aid when used judiciously; first, to render the capsule taut in immature and morgagnian cataracts, so as to facilitate the grasp of the forceps, and second, in aiding the escape of the lens when the section is small or the lens is large. Judgment must be exercised in individual cases, and a capsulotomy should be substituted in certain cases. To avoid the necessity of a discission for an after-cataract, the anterior capsule is best removed by toothed forceps.

7. Complete narrow iridectomy in preference to peripheral iridectomy.

8. Preliminary canthotomy is indicated only to facilitate the extraction in deeply set eyes with small palpebral fissures.

9. The operating room should be quiet, and spectators, if any, should be few. The assistant and the nursing staff should be carefully trained, and should be instructed to observe silence during the operation.

The time element is unimportant if anesthesia is perfect, and the methods suggested are deserving of consideration because of the better results obtainable by the technic as outlined.

DISCUSSION

DR. EDMUND B. SPAETH: There is but little I can add to this paper in its discussion of operative technic, that is, the treatment for cataract in the operating room, but because it has been my fortune to assist Dr. Peter at all of his operative work for the past two years, I have jotted down a few points which might be further stressed.

During this interval of two years, I have watched part of the development of the present technic. This technic is the result of necessity in that, as complications threatened or developed, the mass of advice in the literature was drawn on, utilized as far as possible and amended further by his own originality.

The first point is a willingness to change methods and technic as new factors develop. A mind closed to the happenings of today and to the probabilities of tomorrow would have killed operation for cataract at its birth. Without this willingness to change, the combined extraction would never have been perfected, and intracapsular extraction and the peripheral iridectomy would have died with the demise of their originators. Further development must arise. Test it, if you will, but, in all events, receive it with an open mind.

The second point is, shall I say, the frame of mind in which one approaches both the discussion and the actual execution of the operation.

The operation for cataract is by all surgical rules a major operation, and must be considered as such in the requirements connected with it. Mills, in a recent paper on iris prolapse connected with operation for cataract, summed things up when he stated, "Probably nowhere in ophthalmic surgery has disaster followed neglected application of first surgical principles oftener than in cataract surgery."

Recently, I spoke to a general surgeon, a man of international fame, and asked him if he could tell me in a few words the most important points in surgical

technic. His reply was, "That is easy: anesthesia, regard for tissues, prevention of shock, asepsis, adequate closure of surgical wounds," and then he added with a smile, "and a knowledge of anatomy and of pathology is the most important." He said nothing about manual dexterity, and when asked definitely about this, added, "If those I have just mentioned are fulfilled then manual dexterity must have been present." It seems that a lack of "surgical-mindedness" is the biggest hindrance in this phase of surgery.

The last point I have noted is relative to the use of sutures in the extraction of cataract. Before flap-sutures were used, iris prolapse was entirely too frequent. As soon as an apex suture was used, the incidence of this complication was reduced. It still occurred, however, though less frequently. During the operation, one can see the reason for this. The unopposed pull of the superior rectus causes a gaping of the corneoscleral incision. The operative defect formed by this is in the shape of a crescent, concavity downward. As soon as this suture is placed, this crescent is subdivided into smaller crescents, one lying on each side of a vertical corneal meridan. They are now more nearly triangular, and their convexities are in apposition. On the other hand, with the sutures placed in the outer angles of the incision and at the junction of the outer and middle thirds, the operative wound is snugly closed, so that one has just a bit of difficulty in worming into the lips of the wound a flat irrigation tip or the repository spatula, when this procedure is necessary.

The literature is full of all sorts of strange and bizarre events through which patients have passed in convalescence without damage only by reason of corneal sutures. This past week a patient, aged 82, fell from her bed the night of the extraction of her cataract, without any damage to her eye. She had had two well placed corneoconjunctival sutures. On the other hand, about eight months ago, a patient of a much less advanced age broke open her incision when reaching for the telephone, four days following an uneventful extraction by capsulotomy and iridectomy. Another patient, six days after a similar operation a few months before this, broke open his incision late one night when the nurse flashed a light in his face. As a large incision facilitates proper extraction of the lens without undue pressure on the eye (with a resulting traumatic iritis as its sequela) it seems even more necessary, as this tenet is carried out, that adequate sutures be used. It is a basic rule in abdominal surgery that the incision be sufficiently large to allow for proper manipulations. This is even truer with extractio lentis. If for no other reason than the sealing off of potential infection from the vitreous chamber, sutures are indicated. The mental ease which these give to the operator is not to be lightly dismissed.

FRENCH SOCIETY OF OPHTHALMOLOGY

Annual Meeting, Paris, May 13-16, 1929

Dr. Onfray, *Reporter;* Dr. Percy Friedenberg, New York, *Translator*

First Session, May 13

Professor Van der Hoeve (Leyden), *President, Presiding*

The Astigmatic Pencil and the Three Equations of Sturm. Dr. Dufour, Nancy.

A description is given of a method which allows one to deduce the two first equations of Sturm from the fundamental formula of Gullstrand ($k^2B=A+kD$). The third equation of Sturm merely expresses the fact that the refracted ray remains in the plane of incidence.

THE RELATION BETWEEN THE REFRACTIVE POWER OF A CORRECTING LENS AND ITS POSITION.

The author notes the value of logarithmic paper in the plotting of graphs.

AUTOPHYLACTIC THERAPEUTICS IN OPHTHALMOLOGY. DR. EMIL FEUILÉ, Paris.

The author discusses methods of treatment directed not so much to the eye itself as to the defense mechanisms of the blood. Local treatment is reduced to a minimum. The author's technic consists in intramuscular injections of colloidal silver, mercury and soluble bismuth (milligrams). The purpose is that of resorbtion, activation and leukocytosis with chemotaxis. As ancillary methods we must bear in mind opotherapy by means of thyroid preparations and the use of irradiated ergosterol. In this way a large number of acute as well as chronic ocular conditions are rapidly cured.

ELONGATIO CONGENITALIS CANALICULORUM LACRIMALIUM INFERIORUM CUM ANKYLOBLEPHARON INTERNUM. DR. J. VAN DER HOEVE, Leyden.

The author discusses a condition which represents a hereditocongenital anomaly of familial distribution. The principal features are the excessive length of the lower lacrimal canaliculus and the nasal ankyloblepharon resulting in slight epiphora with some cosmetic disfigurement. The reader of the paper presented a number of portraits of subjects with this anomaly, as well as a family tree in which the father and six of ten children were affected by this anomaly, which, he concludes, is not excessively rare.

PAPILLOMATOUS EPITHELIOMA OF THE NASAL FOSSA TWENTY-FOUR YEARS AFTER EXTIRPATION OF A PAPILLOMA OF THE LACRIMAL SAC. DR. DUPUY-DUTEMPS, Paris.

The author reports the subsequent history of a female patient, then 22 years of age, on whom he operated in 1903. This case of papilloma, presented before the Société d'Ophthalmologie of Paris in 1905, is the only one of its kind on record in the literature. Twenty-four years later, there was the beginning of a nasal obstruction on the same side. One year later, the patient applied for advice and relief from a diffuse swelling at the lower inner margin of the orbit due to a large growth filling the nasal fossa and widely rooted in its outer wall. Removal of the growth and resection of the ethmoid, which was completely invaded, and of the upper inner wall of the antrum followed. The structure of the neoplasm indicates its origin from the original papilloma, parts of which had undoubtedly remained out of reach at the lower extremity of the nasal canal, as papillomatous epithelioma is practically unknown in the nasal fossa.

BIOMICROSCOPY OF THE TARSAL CONJUNCTIVA IN TRACHOMA. DR. CUENOD and DR. ROGER NATAF, Tunis.

Cuenod and Nataf describe a system of newly formed vessels which exists in trachoma from the very beginning as seen with the slit-lamp. The normal vascular network spread out on the tarsus gives rise, at right angles, perpendicularly to its plane, to a large number of small branches each of which spreads into a sort of bouquet on the surface of the thickened mucosa. Other visible branches contribute to the periampullar and intra-ampullar vascularization of the granular follicles. At a later stage (periode d'êtat) the most interesting point to be noted is

the presence, around the granular follicles, of a fine mosaic or marquetry of extremely minute polygonal papillae. This mosaic, of a characteristic appearance and pattern, is seen in every case of pure trachoma examined with the biomicroscope. Each of the polygonal plaques corresponds to one of the aforementioned bouquets of newly formed capillaries.

BACTERIOLOGIC EXAMINATIONS PRECEDING OPERATIONS FOR CATARACT. DR. MOREAU, Saint-Etienne.

The author reports on a series of 100 cases of cataract. Cultures from the conjunctival culdesac on gelose T and gelose Martin showed the following pathogenic micro-organisms: staphylococcus, 40 per cent, of which one-sixth were *S. aureus;* staphylococci and club-shaped bacilli, 9 per cent; no micro-organisms, 19 per cent; mixed, diphtheroid diplobacilli, 10 per cent; pneumococci, some streptococci, 20 per cent, and *Bacillus coli-communis,* 1 per cent. Against the pneumococcus, the most dangerous of these germs, the best recourse is to optochin, 1 per cent, instillations of which are followed by a disappearance of the microbe in four or five days, or to silver nitrate, 1 per cent; treatment with bouillon vaccine does not prevent pneumococcus panophthalmia if the lacrimal passages are not normally permeable. Microscopic control is not enough to give security to the operator, as a patient convalescing from grip, even without pneumococci in the conjunctiva, may develop a pneumococcus panophthalmia. The prophylactic preventive treatment for postoperative suppuration consists, probably, less in doing away with poulticing (simple hot air treatment with the thermophore) than in procedures aiming at sterilization and neutralization of the bacterial flora in the conjunctival sac preliminary to operation.

DISCUSSION

DR. A. J. TERSON: Preoperative bacteriologic examination, whether positive or negative in its results, may leave us in uncertainty as to the successful outcome of the surgical procedure. Accordingly, no matter what the nature of the actual or supposedly dangerous germ, I, guided by the investigations of M. Carrère, use, locally, bouillon vaccines pneumococcus or mixed, and in the presence of ozena, which so markedly disposes to infections, I add pneumococcus vaccine. The latter germ is often present in ozena and forms particularly fetid cultures. I have been struck by the perfect tolerance, by the eye, of vaccine "baths" twice daily for three or four days, alternating the preparations, and by the uniformly good operative results, as to cataract, even in subjects with marked involvement of the lacrimal passages.

VACCINE THERAPY OF GONOCOCCUS CONJUNCTIVITIS. DR. G. RENARD, Paris.

Renard adds to his previously reported series, observations in twenty-three cases of ophthalmia neonatorum in which the patients were treated with the vaccine. In every case, bacteriologic examination had demonstrated the presence of gonococci, and six infants presented evidence, before treatment, of corneal involvement. With the exception of three cases, which could not be followed up, all of the patients recovered completely without sequelae. Renard uses a polyvalent vaccine with *B. pyocyaneus,* which is well tolerated. He gives details as to the procedure and lays stress on the rapid action of the vaccine which dries up secretions in two or three days, but warns that the immunity thus established is of short duration, and that relapses may occur if treatment is stopped too early.

Subconjunctival Injections of Neutral Atrophine Sulphate. Dr. Perrin, Lyon.

Cysts of the Conjunctiva. Dr. L. Carrère, Montpellier.

The author describes a cystic formation of the upper culdesac growing rapidly after sudden appearance. Histologic examination shows a wall composed of cubic or cylindric cells, some of which was muciparous, arranged in one, two or three layers. The content was a clear liquid rich in albumin. As to the pathogenesis of these neoformations which are generally attributed to embryonic inclusion processes, the author shows that we actually have to deal with a form of retention cyst due to occlusion of the efferent duct of one of the glands of Krause, although no glandular structural elements were found in the adjacent tissues.

On Retraction of the Conjunctiva. Dr. E. Redslob, Strasbourg.

Redslob discusses that form of retraction which is generally called essential shrinking of the conjunctiva, first described in 1878 by Graefe, and attributed by von Kries to pemphigus. In certain cases the bullous eruption is strictly limited to the conjunctiva, the skin (and other mucous membranes?) being spared, and the bullae burst a few minutes after their appearance, so that the diagnosis is not always clear. In spite of certain clinical and pathologic discrepancies, this condition is generally attributed to pemphigus. The author reports the case of a man, aged 29, who, since he was 15 years of age, has had crops of bullae on the conjunctiva, buccal mucosa and urethral mucosa, resulting in shrinking of the conjunctiva and a filiform stricture of the urethra. The skin lesions were so protean that the dermatologists made a diagnosis of polymorph dermatitis of Duering-Brocq, a characteristic condition distinct from pemphigus. A further diagnostic and prognostic point of differentiation of this form is its comparatively benign course. In spite of its persistence for upward of fourteen years, neither the vision nor the general condition has been affected.

Vaccinia Pustule of the Eye Cured by Tetraoxydiphosphaminodiarsenobenzol. Dr. Sexe, Besancon.

False Intra-Ocular Foreign Bodies. Dr. H. Coppez, Brussels.

In subjective cases the patient has the sensation of a foreign body in the conjunctival sac or on the cornea, the real trouble being a conjunctivitis, corneal erosion, or the beginnings of a keratitis, iritis or even glaucoma. The disease is often attributed to traumatism, and when it is a question of industrial injury and compensation, legal procedures often follow.

In objective cases the examining physician thinks he sees foreign bodies when in reality there are none. Small masses of iris pigment are mistaken for powder grains or chips of metal. There is discoloration of the iris simulating siderosis. Partial atrophy of the iris gives the impression of a tear due to injury. Thickening of the lens capsule suggests the presence of an encapsulated foreign body, etc. The patient is impressed by the repeated examinations, develops a traumatic neurosis, or tends to confirm the mistaken diagnosis by aggravating his actual visual defect. Even simulation cannot always be excluded.

In cases of actual foreign bodies the surgeon may be misled and mistaken, for a foreign body, some pathologic or even physiologic appearance of the intra-ocular tissues. This mistake in diagnosis is common in cases of double perforation of the eye in which owing to its extra-ocular situs, the foreign body is

inoffensive but has left the traces of its passage through the globe in the form of pigment masses in the choroid which may resemble a metallic splinter.

KERATITIS NEO-NATORUM. DR. BRETAGNE, Nancy.

Bretagne reports the case of a new-born infant who on the sixth day after a normal delivery presented a diffuse infiltration of the cornea with marked opacification particularly of the lower half. After extensive epithelial desquamation the cornea gradually cleared and regained its complete transparency in fifteen days. The suspected silver nitrate drops instilled into the conjunctival sac of a young rabbit produced exactly the same corneal changes. Chemical tests showed that the solution of silver was actually one of 7.5 per cent instead of 1 per cent. The author warns of the danger of nitrate of silver in case of error in dosage or preparation, particularly as to the inadvisability of using solutions which have become concentrated through long standing, as in this case.

CORNEAL EDEMA IN HYPERCHOLESTERINEMIA. DR. AUBINEAU, Nantes.

The author notes that this extremely special and rare form of imbibition is independent of intra-ocular hypertension and of any symptoms of infection. It is characterized by its being marked on awakening in the morning and steadily receding during the day with an accompanying denudation of the corneal epithelium. In all of the cases there was an excess of blood cholesterol. Improvement and cure were possible only by way of diet, cutting down the ingestion of cholesterol. There were, it may be added, no actual deposits of this product, the condition being a disturbance of metabolism resulting in an excess of "humoro-cellular" cholesterol which disturbed the lipoid balance, increased the index of imbibition of the cornea and interfered with its transparency.

TATTOOING OF LEUKOMAS BY INTRA-CORNEAL INJECTIONS. DR. RALLET, Lyons.

For the palliative treatment for dense corneal opacities the author uses a dental syringe with an extremely fine needle, 4/10 mm. bore. In four cases, a sterilized suspension of india ink injected in this way gave satisfactory results.

OCULAR COMPLICATIONS OF DENGUE FEVER. DR. BARGY, Hanoi-Perpignan.

The author notes that diseases of the eye do not often accompany or follow this disease. In seventeen years, Bargy has been able to collect only four cases. There were two cases of corneal herpes, one noted on the fourteenth day of the eruptive fever, the other coming on with each relapse of the systemic disease, three times, in all. There was oculomotor paresis with involvement of accommodation, pupillary action and motility of the upper lid on the twenty-fifth day. Retrobulbar neuritis, with ocular pain, central scotoma and dyschromatopsia occurred on the twenty-sixth day. These ocular complications are characterized by their appearance, uniformly, toward the beginning of convalescence, their fugitive nature, benign course and amenability to treatment, or even spontaneous cure.

Second Session, May 14

SZYMANSKI, Vilna, *Presiding*

REPORT ON THE ETIOLOGY AND TREATMENT OF BLEPHARITIS. DR. AUBARET, Marseilles.

This topic is practically important, as about half of those consulting us have some form of blepharitis. It is also of dermatologic and general pathologic

interest. Conditions of the scalp of the lashes (cuir ciliaire after A. Terson) have been known and described by medical writers under various names since the earliest times, although the term blepharitis did not come into common use until the eighteenth century. Aubaret describes in detail the three important histologic structures: skin, hair follicles and glandular apparatus, which may be studied in vivo with the ocular loupe. From the dermatologic point of view we must bear in mind the preblepharitic significance of disease of the lid margins, whether due to hyperemia, infection, disturbed metabolism, deficiency states or dyscrinisms. Various forms of dermatitis, eczema, acne and so on, may be localized on the lid margin. Glandular forms may result in oily or dry seborrheic blepharitis, such as the meibomian, studied by Krueckman, or the Moll form, with mixed serous and oleagineous secretion. Bacterial invasion gives us the simple, mycotic, acniform or furuncular varieties of follicular blepharitis. The staphylococcus is probably the most important germ in this respect. The acute exanthems, as well as diphtheria, grip, erysipelas, typhoid, less uniformly the chronic infections, syphilis, tuberculosis and lepra, play an important etiologic rôle. The ocular factors are noted, first, in relation to chronic conjunctivitis, trachoma and diseases of the lacrimal passages (dacryoblepharitis) and conditions of the nasal passages (rhinoblepharitis). Errors of refraction, particularly hypermetropia and astigmatism, must be borne in mind. Treatment must be directed primarily to the underlying etiologic factors, the avoidance of irritating secretions, ocular hygiene, protection from smoke, wind, dust and so on. Local treatment consists in the application of salves, massage of lids, expression of infected follicles, epilation and vaccine baths, while much can be done by attention to the general condition, opotherapy and hydrotherapy, the thermal cures, ultraviolet rays, medicated baths and diet. Vitamin deficiencies must be made good with butter, orange juice, cod liver oil, and a disturbed endocrine balance restored if possible. Finally, desensitization in the presence of anaphylaxis and allergy, immunization and paraspecific protein therapy must be considered. Autoserotherapy and autohemotherapy have been used with inconclusive results. The same holds true of autovaccine and stock vaccines.

DISCUSSION

DR. A. TERSON: The dermatologic point of view is of paramount importance. Local irritation, alone, is not a sufficient cause of blepharitis. There must be, in addition, a local sensitization. The clinical subdivisions follow closely those of skin diseases, eczema, sycosis, folliculitis, dermatitis, seborrhea and favus. Treatment, also constitutional as well as local, follows analogous lines also. The gastrointestinal tract must be carefully regulated. Irritating eye washes should be avoided. Mild astringents should be given, weak solutions of silver, zinc, later sulphonated bitumen, N. F., and colloidal sulphur, not the irritating precipitate. Petrolatum alone should be avoided as an excipient, and hydrous wool fat or a combination with cholesterol should be added. Baths of 3 per cent mercuric salicylarsenate, local vaccine baths in certain cases, yellow oxide ointment, massage and expression, are all valuable.

INDICATIONS FOR TARSORRHAPHY. DR. VAN LINT, Brussels.

Van Lint discusses the torpid ulcer and ulcus rodens corneae, traumatic scleral staphyloma and contused perforating wounds of the anterior segment of the globe. In the first class of cases, the author advises this procedure when current methods have failed. In cases of penetrating wounds he considers it preferable to the use of protective conjunctival flaps and thinks that eyes can be saved which otherwise would have had to be enucleated.

DISCUSSION

DR. A. TERSON: I consider tarsorrhaphy as a final resort, a form of permanent elastic poultice and one which is most natural for a sick eye. Still, in place of the ordinary dressings and poultices, it would be well to try hermetic occlusion for a long period by means of strips of zinc oxide adhesive plaster.

MEDIAN, REVERSED V, BLEPHAROTOMY-PALPEBRAL HARELIP ALLOWING VISION AND OCCLUSION OF A SQUINTING EYE. DR. H. TRUC and DR. C. DEJEAN.

Following an epithelioma of the left lower lid, treated repeatedly with radium, the lid had entirely disappeared. The thickened upper lip was drawn down and adherent by cicatricial adhesions at its two ends. The left eye itself, enveloped in scar tissue, was drawn up and fixed under the upper lid in a position of strabismus sursum vergens. As the right eye was sightless, vision could be obtained only by raising the left upper lid with the fingers. In this unusual and desperate situation none of the typical, classic operations could be thought of. The upper lid was split vertically and cut entirely through, producing a median separation in the form of an upside down V. The result was excellent. The pupil was made accessible to light, the cornea remaining protected by perfect covering when the eyes were closed. The patient was able in this way to use his eye for about two years.

TEMPORARY PROSTHESIS IN ANKYLOBLEPHARON. DR. BICHELONNE, Paris.

The author refers to the publication by Professor Kaz in his "Typhliatrie" of excellent results obtained by the use of celluloid shells in xerosis due to trachoma, in corneal leukoma, as well as in symblepharon and ankyloblepharon. Glass shells of various shapes made by the firm of Giron may also be used, similarly, as preliminary or preparatory to the usual artificial eye after such operations as exenteration, amputation of the anterior segment, enucleation, and so on, to make the orbital cavity more receptive and better adapted for the definite prosthesis.

Third Session, May 15

DR. DE METS, Antwerp, *Presiding*

IRITIS FOURTEEN YEARS AFTER EXENTERATION OF FELLOW EYE FOR SEVERE INJURY. DR. JEANDELIZE and DR. GAULT, Nancy.

The authors report a case of acute iritis with severe reaction but without precipitates on Descemet's membrane developing fifteen years after an injury which necessitated, less than two days later, the removal of the anterior segment of the globe. In spite of all investigations, the origin of this iritis could not be determined beyond a doubt. The authors do not think themselves justified in speaking of a sympathetic iritis, especially as a study of the stump which contained membranes showed no trace of the inflammatory process usually found in the sympathizing eye.

BIOMICROSCOPY OF IRIS GAPS IN A GLAUCOMATOUS EYE. DR. HAMBRESIN, Brussels.

The patient, aged 31, presented a hole in the iris of both eyes. In the right eye, the loss of substance was almost one third of the surface of the iris; in the

left, it was smaller. An interesting feature of this case was the presence in both eyes of cordlike strands extending from the iris to an insertion on the posterior surface of the cornea. Each of these strands formed a distinct track throughout its entire length about from 2 to 3 mm. from the periphery of the iris, and extended from 7 to 3 o'clock. The author feels that these iridocorneal strands have a casual connection with the glaucoma, and that they were factors in producing the defects in the stroma of the iris, as they must have caused a more or less constant if varying pull on the iris stroma on the plane of the iris. The patient, it is to be noted, was one of a glaucomatous family.

SENILE CHANGES IN THE ANTERIOR LENS CAPSULE AND PUPILLARY MARGIN. DR. TRANTAS, Athens.

Vogt, four years ago, described an opalescent crown in the intermediary portion of the periphery of the lens capsule, and a disk, somewhat less pronounced, situated in its central portion, with a sort of bluish haze or moldy blotch on the margin of the iris. In three fourths of the cases he attributed these changes to glaucoma in old patients, having seen but twelve cases in four years. In fifteen months, the author has found forty-two cases, in all of which the patients were over 55 years of age and in whom these lesions could be seen with the slit-lamp after dilating the pupil. Glaucoma was coexistent in only 33 per cent of the cases, while more or less pronounced lens opacities were present in 71 per cent, at times associated with central scotoma, depigmentation of the uveal tract and slight corneal opacities. The lesions are of a senile nature. The coincidence of glaucoma is explained by the fact that this condition, too, develops on a basis of senility with chronic lowering of tissue vitality. Trantas also describes an abortive variety (forme fruste) of the discoid opacity, in the form of a number of isolated points near the center of the capsule. This is more common than the typical disk of Vogt. The opalescent senile capsule may, if marked, interfere with sight. Aside from this, removal of the capsule is useful in cataract extraction. Postoperative glaucoma is explained by the frequency of hypertension in aged subjects. It would probably develop as a senile manifestation, even if no operation was performed.

THE DIELECTRIC VALUES OF THE INTRA-OCULAR FLUIDS. DR. LUSSITCH-MATKOVICH, Zagreb.

RELATION OF INTRA-OCULAR TENSION TO ARTERIAL PRESSURE. CLINICAL ASPECT. DR. BAILLIART, Paris.

Patients with arterial hypertension generally show a normal intra-ocular tension. Many patients with glaucoma have no hypertension. Still, arterial hypertension is rather frequent in these subjects, although it is unusual in acute glaucoma. In the prognosis of glaucoma, the blood pressure must be considered. As a rule, one may say that whenever the intra-ocular tension is more than half as high as the diastolic humeral (brachial) pressure, there is imminent danger for the eye.

NOTE ON GLAUCOMA IN INDO-CHINA. DR. BARGY and DR. PERPIGNAN, Tonkin.

Glaucoma is common in the French East Asiatic possessions, amounting to over 2 per cent of all of diseases of the eye. In 719 cases, plus 46 cases of buphthalmos, seen in ten years one fifth were males. The minimum age was 30, and the average age was 55 years, in cases of chronic glaucoma. Of these 719, 464 were absolute glauconias. This is explained by the indifference of the Annamite and his mistaking the condition for cataract, which he knows to be operable. Of 1,675 cases of

blindness, 517, or about 30 per cent, were glaucomatous. Cicatricial changes at the limbus due to trachoma do not seem to play a part, as trachoma is rare in the glaucomatous cases (one-fourth) and the lesions are slight. Syphilis, however, may be an etiologic factor, as more than half of the chronic glaucomas showed a positive Wassermann reaction, and routine serologic examinations would probably give a much higher percentage.

Some So-Called Primary Glaucomas. Dr. F. Terrien and Dr. P. Veil, Paris.

Three Observations of Chronic Glaucoma. Dr. Thibaudet, Lorient.

In one case a Lagrange operation was performed with a final success after postoperative complications (the development of cataract) in a squinting eye necessitating two operative interventions after the sclerecto-iridectomy. In the second case, the patient was treated by Abadie's method, with success for seventeen months, while the fellow eye, operated on by another surgeon, still has the higher tension of the two. In the third case, the patient was treated by Abadie's method, with complete frustration, in both eyes, then, surgically, with partial success. Medical treatment (Abadie) is still worth a trial under the control of constant clinical observation. Chronic glaucoma is serious but develops slowly, surgical intervention is rarely immediately urgent, and there is always time to have recourse to it if the other method fails.

Technic and Indications for Antiglaucomatous Operations. Dr. A. Terson, Paris.

Postoperative Hemorrhages in Glaucoma. Dr. Morax, Paris.

The author notes that we cannot foresee or prevent hemorrhages into the anterior chamber or anterior part of the vitreous in chronic (nonhemorrhagic) glaucoma, coming on in the first three days after operation, and affecting both eyes if the operation was bilateral. The absorption of blood is always slow and may take from two to five months. The outcome is not so serious as might be expected in the weeks immediately following the accident, and the decompressive effect of the operation may not be jeopardized. Still, if the eye has been seriously affected by the glaucomatous process, the prognosis is bad. In one of the cases reported, the patient had nephritis with albuminuric retinitis. In another, the renal function was normal, but arterial tension showed occasional exacerbations of short duration. This must be guarded against, and patients should get hypotensive diet with blood letting.

Treatment of Late Intra-Ocular Infections Following Eliott's Trephining Operation. Dr. Villard, Montpellier, and Dr. Bouniol, Nimes.

A patient, aged 47, with chronic glaucoma trephined successfully, as to both operation and functional result, developed an acute conjunctivitis, thirty-two days after the fistulization. After this slight inflammation, a suppurative iridocyclitis developed with marked rapidity and of such severity as to threaten complete loss of the eye. Within less than twenty-four hours, a fixation abscess was induced by the injection of 1 cc. of turpentine, and the intra-ocular infection promptly subsided. In a few days more the eye was quiet, the vision being 8/10, but there was complete

obstruction of the scleral opening, and, of course, no fistulous scar. While we must not draw conclusions too freely from a single observation, the immediate relief afforded by the fixation abscess would indicate that it is of great value, if promptly induced, in late postoperative infections after trephining.

CONGENITAL SUBLUXATION OF THE LENS IN TWO SISTERS. DR. J. CLERC, Grenoble.

The author notes that this condition not infrequently gives rise to increased intra-ocular tension of a serious nature and obstinate course, leading to rapid loss of vision. It is not easy to foresee or prevent these complications, and subluxations easily become actual dislocations, whence the difficulty of grasping the lens and the danger of attempts at extraction during the period of plus tension. The logical indication is for sclerecto-iridectomie (Lagrange), which operation in the hands of the author gave excellent results in the two cases, sisters, reported.

ATTEMPT TO DIFFERENTIATE A TYPE OF PRESENILE CATARACT. DR. F. KOBY, Bâle.

Koby describes an opacity beginning in the superficial layers of the anterior cortex in the form of more or less horizontal striae. On optical section, with the slit-lamp, the opacities form a chevron, or V, the apex of which reaches the anterior pole of the lens. The dissociation of the lamellae of the anterior cortex is pronounced; vision begins to deteriorate early. The most clearcut cases were those of two patients, aged 33 and 45, who appeared to have some trouble with the endocrine glands, as evidenced by baldness and excessive obesity. The biomicroscopic appearance is the more striking because the rest of the lens is clear in the early stages. Further investigation should show whether or not this form of cataract is due to dyscrinism.

PLANE-BY-PLANE OPHTHALMOSCOPY IN THE UPRIGHT IMAGE. DR. J. GALLOIS, Paris.

Gallois calls attention to the value of the ophthalmoscope, preferably the electrically lighted model, in the study of vitreous opacities and "possible intra-ocular currents." If the retina is seen with the aperture, the plane of the iris is at from + 18 D to + 20 D. The vitreous extends from + 12 D to + 15 D. The direction and extent of displacement of vitreous opacities or of other intra-ocular bodies can be studied, and their exact location determined.

STUDIES OF THE FORM AND STRUCTURE OF THE VITREOUS. DR. DEJEAN, Montpellier.

The author examined with the slit-lamp, normal eyes under mydriasis, and eleven aphacic globes with large discission opening or complete removal of the capsule, with vitreous in the anterior chamber. With the highest magnification possible the vitreous appears to be made up of a framework or scaffolding (charpente) of true, transparent membranes. They are often easy to pick up with the slit-lamp by reason of the minute brilliant light points with which they are studded. In all cases they can be made out as opaline tracks when the light falls on them tangentially. These membranes surround certain small accidental gaps or hernias of the vitreous. These should not be resected as is the classic procedure, but reduced or covered. In this way one avoids escape of the contents.

Fourth Session, May 16

DR. LUNDSGAARD, Copenhagen, *Presiding*

TRANSITORY BLINDNESS DUE TO RETINAL ANGIOSPASM OF MALARIAL ORIGIN. DR. J. SEDAN, Marseilles.

An officer treated off and on for paludism, who had previously taken large doses of quinine, had a violent attack of malarial chills and fever during which blindness came on suddenly and rapidly became complete. There was total retinal ischemia; the arteries were shiny white, without circulation; the veins were bluish, and the retina was pale pink, with marked ocular hypotony. As it was undecided as to whether the condition was due to the malaria or to the quinine, energetic treatment was started with the drug. This brought the vision up to normal after three days of blindness. The arteries, which had been kept under inspection, refilled after a fashion, under the eyes of the surgeon. This direct observation of angiospasm is exceptional, as is the malarial *(not* quinine-toxic) etiology, the uselessness of amyl nitrite, and the three days' duration of blindness due to the retinal spasm and ischemia. The author is reserved in his prognosis as to the fate of the optic nerves which may become atrophic in case of repeated spastic crises particularly if they are of long duration.

GLIOMA OF THE RETINA WITHOUT RECURRENCE AFTER FOUR YEARS. DR. J. CLERC, Grenoble.

The chances of survival after enucleation for glioma depend largely on whether or not the surgical procedure has been carried out early. As the neoplasm must be tracked down rapidly, the author pleads for routine examination of the eyes of the subjects in infant asylums and schools, which, in fact, are at present rarely, if ever, carried out by oculists.

VISION WITHOUT PIGMENT: THE TAPETUM. DR. ROCHON-DUVIGNEAU, Paris.

Dr. Rochon-Duvigneau gave a demonstration of lantern slides.

LIVER TREATMENT OF HEMERALOPIA AND KERATOMALACIA. DR. TRANTAS, Athens.

Trantas notes the therapeutic use of liver in classic Greek medicine and at various times, later, until it was finally looked on as a popular remedy without any other value than that of concentrated nourishment. His first case, in which the patient was cured, was one in which, thirty years ago he was forced to use liver as a last resort in a desperate case of hemeralopia with keratomalacia. Since then he has cured more than 100 patients, in many of whom the condition was severe, by this Hippocratic method. In three cases of keratomalacia in children of which one followed scarlet fever the patients were treated with liver and recovered rapidly. Cod liver oil is decidedly less efficacious in building up these cachectic infants. As liver is specific for even pernicious anemia, it should be given as a routine in all cases of ocular complications, of blood deficiencies, retinitis, hemorrhages, or optic neuritis of anemic origin, as well as in cases of retinitis pigmentosa if only as an adjuvant to stop, as far as possible, the progress of this incurable condition.

RETINAL VENOUS TENSION, CEREBRAL CIRCULATION AND PAPILLEDEMA. DR. J. DUBAR and DR. A. LAMACHE, Paris.

The factor of retinal venous tension is of importance in increased intra-cranial pressure, particularly if associated with choked disk, in relation to the tension of the cerebrospinal fluid. Practically, this is of value in throwing light on certain obstinate forms of headache and points out the way to treatment.

A PROCEDURE FOR THE OPERATIVE CORRECTION OF MONOCULAR STRABISMUS. DR. B. F. BOURDIER, Paris.

The author demonstrated his method on a film which had been shown at Athens during the French exposition. It applies particularly to unilateral operation for deviations of high degree. Late insufficiencies are generally due to retraction, as under the influence of muscular pull the sutures gradually draw back from their insertion in the episclera or even the sclera about the limbus. As an improvement, the author passes his needles through the muscle stump which has been left in situ and forms a loop of heavy silk which holds the reattached muscle firmly against any possible backsliding. The films showed perfect convergence, with normal associated binocular movements in all directions.

MICKULICZ'S DISEASE. DR. LETULLE and DR. DUCLOS, Paris.

The author presented the case of a woman, aged 50, with painless enlargement of the left lacrimal gland, of both parotids, and induration of the left submaxillary gland. The general condition was fairly good and there was no fever. Microscopic examination was made. The author draws an analogy with amygdaloparotidean cysts of embryonic displastic origin, and claims that Mikulicz's disease represents a congenital pathology with subsequent invasion of the gland tissues by tuberculosis.

X-RAY PICTURES OF THE SKULL OF AN INFANT WITH BILATERAL ANOPHTHALMIA. DR. G. BOREL, Neuchatel.

The absence of the eyeballs has no influence on the development or topography of the orbit, so that the radiography is not altered and shows no anomalies. The embryonic eyes of the microphthalmic subject are capable of rapid development in a few weeks. Anophthalmia generally affects the last children born. Consanguinity and particularly maternal inheritance have an influence on its production. There is a concomitant relation between albinism and anophthalmia, the developmental arrest indicated by the other anomalies playing the principal etiologic rôle.

TWO CASES OF CRANIOFACIAL DYSOSTOSIS OF CROUZON. DR. P. PESME, Bordeaux.

The first case of this typical and peculiar facial malformation associated with ocular lesions was that of a boy, aged 7, with a marked frontal boss, decided exophthalmos, prominent arched nose and a protruding lower jaw, vision in the right eye 2/10 and in the left eye, 1/10. There was double postneuritic optic atrophy. Typical radiologic observations were noted: characteristic steeple skull, digitiform impressions, synostosis of cranial sutures, orbital recession and basilar kyphosis. The hereditary factors were insignificant. The second case, that of a precocious male, showed the same marks as to skull, nose and maxilla, but there was no optic nerve atrophy. Death occurred at 5 months, of inanition. Intracranial hypertension is the important etiologic factor for both the changes in the skull and the ocular complications, in this well individualized osseous dystrophy which as Crouzon's disease must be placed in the same category as steeple skull.

ORIGIN OF THE OCULOMOTOR NERVE IN THE CAT. DR. BEAUVIEUX, Bordeaux.

The author noted the still prevalent lack of certainty as to the exact location of the nuclei of the ocular parasympathetic nerve, i. e., the fibers supplying the ciliary muscle and the sphincter pupillae. The data given by Kahler and Pick, Hansen and Voelkers lack precision, and it is doubtful whether the nuclei described by Darkschewitz and Edinger-Westphal are the real centers. Yet clinical and physiologic data require that these centers be found either in the ganglionic centers of the third pair itself or in their immediate vicinity. The cat is particularly adapted for this study, as pupillary and accommodation movements predominate markedly over extrinsic muscular reactions. Anatomic study of the mesencephalon of this animal shows that the nuclei of origin are formed by a main mass in the form of a horse-shoe made up of large cells which give rise to fibers, most of which are direct, although some, the great minority, are crossed. There is besides, in the hollow of this cellular mass, a small nucleus with pale cells, a single, median nucleus. The author gives the relations of these nuclei to the anterior corpora quadrigemina, the posterior longitudinal bundle, the nucleus ruber, and the rubro-medullary bundle. The description tallies fairly well with that given, for man, by Bechterew, but the final conclusion is that this study has given no definite and final localization of the nuclear centers sought.

DIAGNOSTIC PUNCTURE OF THE HYPOPHYSIS. DR. J. BOURGET, Paris.

Doubt may exist in some cases, as extrasellar tumors may give a similar clinical symptomatology. The choice of an operative procedure, intranasal or via the cranial vault, is also undecided. Bourget punctures and aspirates the hypophyseal gland by the endonasal route after breaking down the bony wall of the sella and exposing the fibrous portion behind which the gland is hidden. The tissue plug thus obtained is hardened, fixed and examined microscopically. While awaiting the laboratory report one has, as it were, made a sellar decompression and can proceed by this route to complete exenteration if the mass is found to be a tumor, or, in the opposite event, reach the suprasellar regions by cranial trephining higher up.

LOCALIZATION OF THE SENSE OF OBSTACLES IN THE BLIND. DR. BENOIT, Paris.

The author studied the peculiar special sense which enables the sightless to detect the presence of a body in front of them or at the side in walking, or when standing still to feel the quiet and noiseless approach of an object, the sensation persisting even when subject and object have come to a standstill. The perception takes place at head level and is limited to the front and sides. The author concludes that this phenomenon is not due to actual tactual sensations, nor to differences of pressure in the surrounding air, nor to auditory sensations communicated to the ear. It is probably a special perception localized in the "mucocutaneous regions innervated by the sensory intracranial nerves." The stimulus is received and transmitted by the free nerve terminations in the epidermis.

TECHNIC AND INDICATIONS IN OPERATIONS FOR GLAUCOMA. DR. TERSON, Paris.

The principles laid down by Graefe and Lagrange must be made more definite and precise, while, in certain special cases, variation is indispensable, if we wish to avoid immediate accident or unsatisfactory results. In ordinary acute glaucoma, iridectomy through the simple scleral incision is probably the operation of choice. But the incision, which can be easily measured by a special squint hook, should not exceed 6 mm. instead of being indefinite in size. A narrow bladed knife is better

than the lance shaped keratome. Double suspension-fixation, the addition of a conjunctival flap, good local anesthesia, and fixation forceps with rounded points so as not to tear the conjunctiva, are factors in perfecting the operation. When it is impossible to enter the shallow or practically empty anterior chamber, a shorter, 5 mm. incision is begun, externally with a Stilling knife and completed with Stevens' scissors. In chronic glaucoma, Lagrange operation, with 5 mm. incision, is advisable. Eliott's trephining is reserved for cases with a shallow anterior chamber, and other special indications, such as buphthalmos and dislocation of the lens.

Book Reviews

DIE BEDEUTUNG DER TUBERCULOSE FÜR DIE ENTZÜNDLICHEN ERKRANKUNGEN DES UVEAL TRACTUS. By DR. JOSEF URBANEK, Assistant First University Eye Clinic, Vienna, with an introduction by Prof. J. MELLER, dedicated to the memory of J. VON MICHEL. Price, 8 marks. Pp. 147, with 79 illustrations. Berlin: S. Karger, 1929.

This is number 12 of the "Abhandlungen aus der Augenheilkunde und ihren Grenzgebieten," which appear as separate monographs of the Zeitschrift fur Augenheilkunde. It is the second treatise of the series devoted to ocular tuberculosis, which demonstrates the importance of the subject at the present day. The subject matter deals principally with diagnosis and "tebeprotin."

Our views on tuberculosis in ophthalmology must change; the tuberculous patient does not necessarily look cachectic, on the contrary, many look the picture of health. No age is free. The results of examination by the internist are often negative, because physical signs are slight; even roentgengrams do not always show lesions.

The subcutaneous injection of tebeprotin and the intracutaneous injection of tuberculin (Mantoux) are of equal importance in the detection of tuberculosis as the Wassermann reaction is for syphilis.

Tebeprotin was discovered by Prof. Toennissen and enthusiastically introduced by Prof. Bruno Fleischer, in Erlangen, and endorsed by many others; still here in the United States, we are prevented from giving it a fair trial because a biologic product cannot be imported.

Tebeprotin is chemically made from virulent cultures of the typus humanus grown on glycerin bouillon. It is a white powder, easily soluble in alkalis, unsoluble in neutral or acidified water. The protein is dissolved in a salt solution, isotonic for human blood; a 0.5 per cent phenyl solution is added for preservation. The pure protein contains 12.6 per cent nitrogen, no phosphorus and no purine bases. Tebeprotin is free from tuberculotoxins. The mortal dose for guinea-pigs is 15 mg.; it kills like the old tuberculin of Koch through focal reaction, not through anaphylaxis.

Its dosage can be more exact, and it acts stronger, that is, in smaller doses, than tuberculin O. Its action cannot be predicted as this depends on the patient's constitution.

Formerly using tuberculin O. for diagnosis, occasionally deleterious focal reaction in the eye occurred, which remained irreparable. With tebeprotin more distinct local as well as general reactions are provoked, and are followed by a higher but shorter lasting rise in temperature. Focal reactions occur in the eye, but in more than 500 cases no permanent damage has occurred, and in many cases the reaction was followed by improvement.

A proof for the specific action is seen in the "reaction-time," which is the same as the reaction-time found by von Frisch for old tuberculin. Until a year ago 0.1 mg. was injected subcutaneously, the temperature taken every two hours for two days, and repeated six

days later if the outcome was doubtful or the process had reacted favorably. During the last year endodermal injections were made with graduated solutions to find out the degree of allergy, and treatment was begun with subcutaneous injections of the strength, which had given a reaction.

Tebeprotin has great diagnostic value; it can be used as a prophylactic when an eye is to be operated on and for therapeutic purposes. In the latter, the dose is gradually increased with lengthening of the intervals, the highest dose never exceeding 0.1 mg., but this is continued for at least a year.

The results are satisfactory; when followed up in the right way pronounced, even excellent, results occur in numerous cases. Improvements are seen daily. However, it is conceded that we are not yet so far advanced that the results in all cases will be favorable nor are we sure of the origin. The treatment may have no effect, but this is the exception. Besides the improvement of the ocular tuberculosis, the primary focus may not be so favorably influenced; this explains later relapses. When loss of central vision is threatened, mercury inunctions are started immediately as tuberculin needs some time before showing any action; besides it seems the metallic products act as sensitizers for tuberculin.

The following conditions are treated: acute and chronic iritis and iridocyclitis; the vascular conditions such as periphlebitis tuberculosa with recurrent hemorrhages in vitreo, and in a most serious form as thrombosis venae centralis, which show favorable influence by treatment with tebeprotin; some forms of abducens paralysis as the result of a localized meningitis; retrobulbar neuritis with central scotoma which is the continuation of the anterior bulbar process or is due to a dissemination from the blood stream directly into the optic nerve; heterochromia iridis. The last of these conditions has been described in cases from the Meller Clinic by Dr. Clarence King, of Cincinnati, in the Transactions of the American Ophthalmological Society, 1927. One case was observed with discoloration of both irides after cyclitis a desideratum mentioned by H. Gradle (*Am. J. Ophth.* **12:** 593 [July] 1929).

Eleven pages are given up to the treatment and many clinical histories illustrate the text.

This review should be compared with that which appeared in the *British Journal of Ophthalmology,* August, 1929, p. 429. It will be interesting to see if the appreciation of the frequent tuberculous genesis of ocular diseases will go the same route as the Journal took when the slit-lamp examination became known.

E. E. Blaauw.

Directory of Ophthalmologic and Otolaryngologic Societies *

FOREIGN

OXFORD OPHTHALMOLOGICAL CONGRESS

Master: Dr. A. B. Cridland, Salisbury House, Chapel Ash, Wolverhampton. England.
Secretary: Dr. C. G. Russ-Wood, 12 St. John's Hill, Shrewsbury, England.

NATIONAL

AMERICAN MEDICAL ASSOCIATION, SECTION ON OPHTHALMOLOGY

Chairman: Dr. T. B. Holloway, 1819 Chestnut St., Philadelphia.
Secretary: Dr. William C. Finnoff, Imperial Bldg., Denver.
Place: Detroit. Time, 1930.

AMERICAN ACADEMY OF OPHTHALMOLOGY AND OTO-LARYNGOLOGY

President: Dr. Harris P. Mosher, 828 Beacon St., Boston.
President-Elect: Dr. William H. Wilder, 122 S. Michigan Ave., Chicago.
Executive Secretary: Dr. William P. Wherry, Medical Arts Bldg., Omaha.
Place: Atlantic City, N. J. Time: Oct. 21-25, 1929.

AMERICAN OPHTHALMOLOGICAL SOCIETY

President: Dr. W. Campbell Posey, Radnor, Pa.
Secretary: Dr. Emory Hill, 501 E. Franklin St., Richmond, Va.

LOCAL

LOS ANGELES COUNTY MEDICAL SOCIETY, SECTION ON OPHTHALMOLOGY AND OTOLARYNGOLOGY

President: Dr. Harold S. Muckleston, 6422 Hollywood Blvd., Los Angeles.
Secretary-Treasurer: Dr. J. Frank Friesen, 1208 Roosevelt Bldg., Los Angeles
Place: California Lutheran Hospital, Assembly Room. Time: 8 p. m., first Monday of each month.

MEDICAL SOCIETY OF THE DISTRICT OF COLUMBIA, SECTION OF OPHTHALMOLOGY AND OTO-LARYNGOLOGY

Chairman: Dr. Louis S. Greene, 1710 Rhode Island Ave. N. W., Washington.
Secretary: Dr. R. E. Gookin, Medical Science Bldg., Washington.
Place: 1718 M St. N. W. Time: 8 p. m., third Friday of each month.

ATLANTA ACADEMY OF OPHTHALMOLOGY AND OTO-LARYNGOLOGY

President: Dr. H. F. McDuffie, 45 Edgewood Ave., Atlanta, Ga.
Secretary: Dr. Leon E. Brawner, 157 Forrest Ave. N. E., Atlanta, Ga.
Place: Academy of Medicine, 38 Prescott St. N. E. Time: 8 p. m., last Thursday of each month.

---

* Secretaries of societies are requested to furnish the information necessary to make this list complete and to keep it up to date.

EYE, EAR, NOSE AND THROAT CLUB OF GEORGIA

President: Dr. George B. Smith, Rome.
Secretary-Treasurer: Dr. William O. Martin, Jr., 478 Peachtree St., Atlanta, Ga.

INDIANA ACADEMY OF OPHTHALMOLOGY AND OTO-LARYNGOLOGY

President: Dr. Albert E. Bulson, 416 W. Berry St., Fort Wayne, Ind.
Secretary: Dr. Robert J. Masters, 601 Hume-Mansur Bldg., Indianapolis.
Place: French Lick Springs Hotel. Time: December 12 and 13, 1929.

INDIANAPOLIS OPHTHALMOLOGICAL AND OTO-LARYNGOLOGICAL SOCIETY

President: Dr. Robert J. Masters, Hume-Mansur Bldg., Indianapolis.
Secretary: Dr. Kenneth L. Craft, Hume-Mansur Bldg., Indianapolis.
Place: University Club. Time: 6:30 p. m., second Thursday of each month from October to May.

NEW ORLEANS OPHTHALMOLOGICAL AND OTOLOGICAL SOCIETY

President: Dr. M. Earle Brown, Maison Blanche, New Orleans.
Secretary-Treasurer: Dr. W. A. Wagner, Pere Marquette Bldg., New Orleans.
Place: Eye, Ear, Nose and Throat Hospital. Time: 8 p. m., third Thursday of each month from September to June.

BALTIMORE MEDICAL SOCIETY, SECTION ON OPHTHALMOLOGY

Chairman: Dr. Leo J. Goldbach, 1012 N. Charles St., Baltimore.
Secretary: Dr. Angus Lloyd MacLean, Johns Hopkins Hospital, Baltimore.
Place: Medical and Chirurgical Faculty, 1211 Cathedral St. Time: 8:30 p. m., fourth Thursday of each month from October to May.

NEW ENGLAND OPHTHALMOLOGICAL SOCIETY

President: Dr. W. Holbrook Lowell, 82 Commonwealth Ave., Boston.
Secretary-Treasurer: Dr. E. B. Dunphy, 520 Commonwealth Ave., Boston.
Place: Massachusetts Eye and Eye Infirmary, 243 Charles St., Boston. Time: 8 p. m., third Tuesday of each month from November to April, inclusive.

DETROIT OPHTHALMOLOGICAL CLUB

Chairman: Members rotate alphabetically.
Secretary: Parker Heath, David Whitney Bldg., Detroit.
Time: 6:30 p. m., first Wednesday of each month.

THE MINNESOTA ACADEMY OF OPHTHALMOLOGY AND OTO-LARYNGOLOGY

President: Dr. C. N. Spratt, 900 Nicollet Ave., Minneapolis.
Secretary-Treasurer: Dr. J. H. Morse, 80 S. 7th St., Minneapolis.

KANSAS CITY SOCIETY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President: Dr. L. R. Forgrave, Logan Bldg., St. Joseph, Mo.
Secretary: Dr. A. E. Eubank, Argyle Bldg., Kansas City, Mo.
Time: Third Thursday of each month from September to May. The November, January and March meetings are devoted to clinical work.

ST. LOUIS OPHTHALMIC SOCIETY

President: Dr. William H. Luedde, Metropolitan Bldg., St. Louis.
Secretary: Dr. Leo L. Mayer, Carleton Bldg., St. Louis.
Place: St. Louis or Washington University Cafeteria.
Time: 6:30 p. m., fourth Friday of each month from October to April, inclusive.

OMAHA AND COUNCIL BLUFFS OPHTHALMOLOGICAL AND OTOLARYNGOLOGICAL SOCIETY

President: Dr. Charles M. Swab, Medical Arts Bldg., Omaha.
Secretary-Treasurer: Dr. J. C. Davis, 1615 Howard St., Omaha.

ACADEMY OF MEDICINE OF NORTHERN NEW JERSEY, SECTION ON EYE, EAR, NOSE AND THROAT

Chairman: Dr. Frederick J. Wort, 1080 Broad St., Newark.
Secretary: Dr. Earl LeRoy Wood, 31 Lincoln Park, Newark.
Place: 91 Lincoln Park South. Time: 8:45 p. m., second Monday of each month.

BROOKLYN OPHTHALMOLOGICAL SOCIETY

President: Dr. Robert M. Rogers, 680 St. John's Pl., Brooklyn.
Secretary: Dr. William F. C. Steinbugler, 515 Ocean Ave., Brooklyn.
Place: Kings County Medical Society Bldg., 1313 Bedford Ave. Time: Third Thursday of February, April, May, October and December.

EASTERN NEW YORK EYE, EAR, NOSE AND THROAT ASSOCIATION

President: Dr. John P. O'Keefe, 251 State St., Albany.
Secretary-Treasurer: Dr. Arthur F. Holding, 142 Washington Ave., Albany.

BUFFALO OPHTHALMOLOGIC CLUB

President: Dr. E. E. Blaauw, 190 Ashland Ave., Buffalo.
Secretary-Treasurer: Dr. A. F. Luhr, Medical Arts Bldg., Buffalo.

NEW YORK ACADEMY OF MEDICINE, SECTION OF OPHTHALMOLOGY

Chairman: Dr. E. F. Krug, 12 W. 44th St., New York.
Secretary: William F. C. Steinbugler, 815 Park Ave., New York.
Time: 8:30 p. m., third Monday of every month from October to May, inclusive.

ROCHESTER EYE, EAR, NOSE AND THROAT SOCIETY

Chairman: Dr. Frank Barber, 75 S. Fitzhugh St., Rochester, N. Y.
Secretary-Treasurer: Dr. Cecil B. Hert, 29 N. Goodman St., Rochester, N. Y.
Place: Rochester Medical Assn., 113 Prince St. Time: 8 p. m., third Monday of each month from October to May.

NORTH DAKOTA ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President: Dr. George M. Constans, Bismarck.
Secretary-Treasurer: Dr. F. L. Wicks, Valley City.

CLEVELAND ACADEMY OF MEDICINE, SECTION OF OPHTHALMOLOGY AND OTO-LARYNGOLOGY

Chairman: Myron Metzenbaum, Rose Bldg., Cleveland.
Secretary: Dr. A. D. Ruedemans, Euclid and E. 93d St., Cleveland.
Place: Winton Hotel. Time: Fourth Friday of each month.

OMAHA AND COUNCIL BLUFFS OPHTHALMOLOGICAL AND OTOLARYNGOLOGICAL SOCIETY

President: Dr. Charles M. Swab, Medical Arts Bldg., Omaha.
Secretary: Dr. J. C. Davis, 1615 Howard St., Omaha.
Place: Medical Arts Tea Room. Time: 5:15 and 7:00 p. m. Third Wednesday of each month from October to May.

OREGON ACADEMY OF OPHTHALMOLOGY AND OTO-LARYNGOLOGY

President: Dr. Joseph L. McCool, 909 Stevens Bldg., Portland.
Secretary-Treasurer: Dr. Andrew J. Browning, 418 Mayer Bldg., Portland.
Place: Good Samaritan Hospital. Time: Third Tuesday of each month.

THE PITTSBURGH OPHTHALMOLOGICAL SOCIETY

President: Dr. Edward B. Heckel, Jenkins Arcade Bldg., Pittsburgh.
Secretary: Dr. George H. Shuman, Park Bldg., Pittsburgh.
Place: Pittsburgh Academy of Medicine Bldg. Time: Fourth Monday of each month, except June, July, August and September.

THE PITTSBURGH SLIT-LAMP SOCIETY

President: Dr. W. W. Blair, 121 University Pl., Pittsburgh.
Secretary: Dr. George H. Shuman, Park Bldg., Pittsburgh.
Place: 121 University Pl. Time: Second Monday evening of every month, except June, July, August and September.

PACIFIC COAST OTO-OPHTHALMOLOGICAL SOCIETY

President: Dr. Arthur Jones, 105 N. 8th St., Boise, Idaho.
Secretary-Treasurer: Dr. Walter F. Hoffman, 817 Summit Ave., Seattle.

COLLEGE OF PHYSICIANS, PHILADELPHIA, SECTION ON OPHTHALMOLOGY

Chairman: Dr. C. E. G. Shannon, 17th and Walnut Sts., Philadelphia.
Clerk: Dr. Alexander G. Fewell, 1924 Pine St., Philadelphia.
Time: Third Thursday of every month from October to April, inclusive.

SOUTHERN MEDICAL ASSOCIATION, SECTION ON EYE, EAR, NOSE AND THROAT

Chairman: Dr. William Thornwall Davis, 927 Farragut Sq., Washington, D. C.
Secretary: Dr. Fletcher D. Woodward, Box 162, University, Va.
Place: Miami, Fla. Time: Nov. 20-22, 1929.

THE MEMPHIS SOCIETY OF OPHTHALMOLOGY AND OTO-LARYNGOLOGY

Chairman: Each member, in alphabetical order.
Secretary: Dr. R. O. Rychener, Exchange Bldg., Memphis, Tenn.
Place: Eye Clinic of Memphis Eye, Ear, Nose and Throat Hospital. Time: 8 p. m., second Tuesday of each month.

DALLAS ACADEMY OF OPHTHALMOLOGY AND OTO-LARYNGOLOGY

President: Dr. D. L. Bettison, Medical Arts Bldg., Dallas, Texas.
Executive Secretary: Dr. W. Mood Knowles, Medical Arts Bldg., Dallas, Texas.
Recording Secretary: Dr. L. A. Nelson, 4105 Live Oak, Dallas, Texas.
Place: Dallas Athletic Club. Time: 6 p. m., first Tuesday of each month from October to June. The November, January and March meetings are devoted to clinical work.

FORT WORTH EYE, EAR, NOSE AND THROAT SOCIETY

President: Dr. C. P. Schenck, Medical Arts Bldg., Fort Worth, Texas.
Secretary-Treasurer: Dr. R. H. Needham, Fort Worth National Bank Bldg., Fort Worth, Texas.
Place: University Club. Time: 6:30 p. m., first Friday of each month except July and August.

HOUSTON ACADEMY OF MEDICINE, EYE EAR, NOSE AND THROAT SECTION

President: Dr. John H. Foster, 1300 Walker Ave., Houston, Texas.
Secretary: Dr. Edward W. Griffey, Houston Clinic, Houston, Texas.
Place: Medical Arts Bldg., Harris County Medical Society Rooms. Time: 8 p. m., first Thursday of each month from September to June.

THE SAN ANTONIO OPHTHALMOLO-OTO-LARYNGOLOGICAL SOCIETY

President: Dr. F. H. Roseborough, 302 Moore Bldg., San Antonio, Texas.
Secretary-Treasurer: Dr. William D. Gill, 323 Medical Arts Bldg., San Antonio, Texas.
Place: Bexar County Medical Library. Time: 8 p. m., first Tuesday of each month from October to May.

PUGET SOUND ACADEMY OF OPHTHALMOLOGY AND OTO-LARYNGOLOGY

President: Dr. Will Otto Bell, Medical-Dental Bldg., Seattle.
Secretary-Treasurer: Dr. Francis A. Brugman, Medical-Dental Bldg., Seattle.
Time: 8 p. m., third Tuesday of each month, except July and August.

NASHVILLE ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

Chairman: Dr. Herschel Ezell, Doctor's Bldg., Nashville, Tenn.
Secretary-Treasurer: Dr. W. W. Wilkerson, Jr., Bennie-Dillon Bldg., Nashville, Tenn.
Place: St. Thomas Hospital. Time: 8 p. m., third Monday of each month.

UTAH OPHTHALMOLOGICAL SOCIETY

President: Dr. F. M. McHugh, 17 Exchange Pl., Salt Lake City.
Secretary-Treasurer: Dr. H. Leroy Smith, Ezra Thompson Bldg., Salt Lake City.

VIRGINIA SOCIETY OF OTO-LARYNGOLOGY AND OPHTHALMOLOGY

President: Dr. H. B. Stone, Roanoke.
Secretary-Treasurer: Dr. Fletcher D. Woodward, Box 162, University.

SPOKANE ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President: Dr. O. M. Rott, Paulsen Bldg., Spokane Wash.
Secretary: Dr. C. A. Veasey, Jr., Spokane, Wash.

THE MILWAUKEE OTO-OPHTHALMIC SOCIETY

President: Dr. L. P. Allen, 145½ Main St., Oshkosh, Wis.
Secretary-Treasurer: Dr. Edward R. Ryan, 425 E. Water St., Milwaukee.
Place: University Club. Time: 6:30 p. m., third Tuesday of each month.